THE QUARTERLY REVIEW *of* BIOLOGY

VOLUME VIII
1933

Published by

THE WILLIAMS & WILKINS COMPANY
BALTIMORE
U. S. A.

THE QUARTERLY REVIEW OF BIOLOGY

CONTENTS

VOL. VIII, NO. 1 MARCH, 1933

THE QUARTERLY REVIEW of BIOLOGY

THE MOLECULE IN BIOLOGICAL STRUCTURES AS DETERMINED BY X-RAY METHODS

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THE intimate structure of organized bodies has been for a long time a fascinating field for speculation among biologists, especially among those who are interested in growth and functions of living organisms. It was thought that knowledge of this nature would make clearer an understanding of the mechanisms of vital processes. Nägeli's attempts (1) in 1858 were among the first to explain properties of biological structures by means of a molecular hypothesis, although he preferred to think in terms of molecular aggregates which he called micelles, particles composed of several thousand molecules. His conceptions based on growth, swelling and optical phenomena have stimulated investigations along many lines, even up to the present day; however, it was not until the first of the present century that the micelle became a physical reality. This was due to the invention of the ultramicroscope. The molecule and the atom remained for the most part "convenient mental abstractions having no actual existence," until about twenty years ago. At that time, to the physicist at least, they became actual particles with fairly definite structures and properties. The demonstration of their existence did not come as a surprise to many physicists and chemists, for numerous investigations had already strongly indicated their reality, which, however, awaited the brilliant work of Laue and his colleagues (2) for confirmation. They were able, by making use of crystals as diffraction gratings for X-rays, not only to show that atoms and molecules were physical entities, but also to open new fields for investigation in many branches of science; and as a result, physicists and chemists at the present time seem far more satisfied with their conceptions of molecules than are many biologists with their notions concerning centrosomes, mitochondria, genes and filtrable viruses. In spite of the fact that molecules are far below visibility with the most powerful microscope, for the smallest visible particle may be a thousand or more large molecules in diameter, it is possible by means of X-ray crystal structure methods to measure these minute entities with a considerable degree of accuracy, and in many cases to show the relative position

of their component atoms. From this information it is now possible to make models of molecules, built to scale, large enough for more leisurely study; and since the molecule as a unit of structure is more simple than the biological cell as a unit, there seems to be a possibility of gaining a somewhat clearer comprehension of the living organism through studies of these models.

As mentioned above, X-radiation is involved in these investigations. Its value for biological investigations in a somewhat different capacity was recognized almost immediately upon its discovery, made by Roentgen in 1895, for a radiation which would allow a visual examination to be made of the bones in a living body was of too great importance to be overlooked by the surgeon. At first it was thought that the rays had no ill effects on the body; but it was not long before serious flesh burns were found to be caused by this new radiation, and with this discovery a new property of X-rays came forcibly to the attention of the biologist. These two properties, penetration of opaque materials, and injury to living tissues, held the attention of the biologist for nearly three decades. During that time the physicist was studying the X-rays themselves, and was finding them to be a prolific source of information concerning the atom and the structure of matter. Through his discoveries a third field was opened up to the biological investigator, that of studying physically the molecular structure of plant and of animal tissues. Research in this field has not developed very far up to the present time, principally because the technique is complicated and demands a training involving phases of physics and chemistry for which biologists in general do not seem to feel the need. Nevertheless, the work seems important enough to warrant a review, in which an attempt is made to show, in a fairly simple way, the methods and processes involved in these molecular studies, and to give a brief account of some of the results obtained.

Each of the three fields of investigation mentioned is associated primarily with a particular characteristic of X-radiation, and for that reason, some of the properties of X-rays are mentioned here briefly, merely to recall them to mind (3, 4). In attempting to characterize X-rays in a few words, it may be said that they are electromagnetic waves of very short wave-length. The size of the wave-length makes possible the shadow photographs of the surgeon; the electromagnetic nature of the radiation is associated with the effect upon living matter; and the characteristics of the waves as such are brought into direct use in molecular structure investigation. Of course, the characteristics of waves are not to be considered as completely separate from the electromagnetic effects, nor from wave-length, but the apparent predominance of one characteristic over the others has resulted in three types of investigation each having its own particular technique.

We may think of a beam of X-rays as consisting of waves of many different wave-lengths ranging from approximately 0.2 Ångström unit (an Ångström unit is 10^{-8} cm. or $\frac{1}{10,000,000}$ mm.) to about 2.0 Å, as opposed to visible light, in which the wave-lengths are several thousand times as long. Due to its short wave-length X-radiation is enabled to penetrate opaque substances. The shorter the wave-length, the "harder" the ray is said to be, and the greater is its penetrating power. On the other hand the "soft" ray is of longer wave-length and does not penetrate so deeply. The power of penetration varies not only with the wave-length but also with the substance. In other

words, the penetrating rays are absorbed to a greater extent in one substance than in another. It is due to this ability of X-rays to penetrate substances, and in addition, to the ability of the substances to absorb the rays differentially, that shadow pictures of one substance embedded in another are made possible. The well known photographs of bones and teeth are examples of such pictures.

The electromagnetic nature of X-ray waves leads one to anticipate disturbances of some kind in the minute electrical systems of the component atoms and molecules of substances, when they are irradiated. Such disturbances might well be expected to occur in active protoplasm, where metabolic reactions are so nearly balanced. One may think of these reactions as occurring in some orderly fashion, and when a disturbance is produced, the routine of the reactions may be changed, resulting in new structural or other developments. Practically nothing of the nature of these disturbances is understood, and a molecular picture of the mechanisms which are involved in X-ray burns, and in mutations in genetical investigations, is at present decidedly vague; but in spite of that, the work that is being carried on in these fields, while necessarily empirical, seems to be yielding rich returns. The situations involved, however, are of such great complexity that a clear understanding of the reactions seems to be a matter of the distant future.

The wave properties of X-radiation and the minute size of its wave-lengths are characteristics which have made X-rays a powerful tool with which to investigate the structure of matter. Direct evidence has been obtained of the existence of atomic and molecular entities. The investigations have shown that the atom occupies space corresponding to a sphere of about 1.5 Å to 2.5 Å in diameter, and that the size of the atom for a given element is fairly constant, varying only slightly in different types of molecules. Investigations (4) have brought out the concept of the molecule as a group of atoms which are held strongly together into a single entity; and considerable information has been obtained concerning the relation of molecules spatially to one another, the distances which separate them, their sizes, shapes and orientations. Still further, with the help of data from sources other than X-rays, it has been possible to determine the arrangement of the atoms within the molecule itself. In practically all cases, solid crystalline materials were employed for investigation; relatively very little work has been done on liquids and colloidal systems.

The methods used to demonstrate these facts concerning molecular structure were based upon physical and crystallographic theories, and brought together the wave theory of light, the lattice theories of crystal structure, and more commonly known physical and chemical laws. The procedure in these investigations is an outgrowth of the early successful attempts of Laue, Friedrich and Knipping in 1912 to use a crystal as a diffraction grating for X-rays (2); and of the work in the same year of Sir William Bragg and W. L. Bragg in simplifying the method (4).

The importance attached to these discoveries is indicated by the great number of investigations reported since that time (3); hundreds of crystals have been examined and their "fine" structure, that is, their atomic or molecular structure, determined. By far the greater number of these reports has dealt with inorganic crystals and metals; only relatively few organic crystals and a still smaller number of biological structures have been investigated. The work done on organic crystals is of direct, although of secondary in-

terest to the biologist since it is through the structure of the individual organic crystal that a knowledge of the existence of the individual molecule as an entity is obtained.

In 1923 it was shown that, in all probability, in the benzene crystal the six-carbon benzene ring represented the unit of structure (5) just as the individual brick in a brick wall is the unit. Shortly thereafter, in the carbohydrates, the six-carbon group was shown also to be the unit (6), and in fatty acid crystals the long hydrocarbon chain proved likewise to be a structural entity (7). The methods used were found to be applicable to biological materials; and when applied to the solid components of organisms, especially those parts which seemed to be layered in structure, they have given noteworthy results. Among structures of this type cellulose, as found in the wall of plant cells, has been perhaps the one most extensively investigated, although a dozen or more biological substances have been examined. A list of such substances includes starch grains, chitinous plates, tunicin, hair, wool, feathers, quills, muscle tissue, hemicelluloses, and a few structures such as bone, dentine, eggshell, etc. Substances which might be classified as by-products of metabolism or as being associated in some less direct way with the organism, such as rubber, gelatin, and glue have also received more or less attention.

Before attempting to give the results obtained by various investigators in their work with the substances just mentioned, a description of the procedure used in determining the molecular structure of these materials by X-ray analysis is presented. No attempt is being made to describe the work in all of its details; instead, it is hoped that the discussion will bring out the underlying principles and in the end give a picture of the molecule whenever the investigations have proceeded far enough. Concepts of X-ray physics, crystallography, and organic chemistry are involved, and it is likely that the terminology of these three fields may creep into the discussion; however, the effort is being made to make the descriptions intelligible to those who are not familiar with the jargon of one or another of these specialized branches of science. Minute exactness will undoubtedly suffer at the expense of more readily attained conceptions, but should the details be desired, it is hoped that the references cited will either provide the information or will lead to references which will furnish it. The literature is so extensive that only references which seem to be essential are given.

The experimental methods and the procedure which were used in interpreting the data for the various steps employed in determining the structure of cellulose, are taken here as more or less illustrative examples of the work done on biological materials in general, since they embody certain details of technique which are likely to be applicable to other organized structures.

In the studies of cellulose many kinds of plant cells were examined but the fiber was found to be the type best suited for intensive study. Bast fibers of ramie, *Boehmeria nivea*, have proved more useful than have other fibers such as tracheids of wood, hairs of cotton or bast-fibers of flax and hemp; these, however, have the same molecular structure.

The problem at hand, then, is to obtain a conception or picture of the molecules of cellulose, and of their arrangement in the wall of a fiber. The picture is built up bit by bit from the interpretations of experimental data obtained primarily through X-ray crystal structure methods (8). With suitable apparatus records, usually photographic, were obtained of beams of X-rays

which had been reflected from layers of atoms occurring in the wall of the fiber. Interpretation of these records made it possible to construct a geometric model showing the arrangement of the molecules. In order to make clear the method of obtaining the photographic data and of interpreting the latter, the various steps in the process will be taken up under several headings which will be seen to lead progressively to a conception of the molecular structure.

A great deal of the work is associated with a fundamental relationship which exists between three things: the X-rays, the angle at which the beam impinges on the fibers, and the distance between the layers of atoms in the fiber. Three quantities are involved in this relationship, the wave-length of the X-ray waves, which is designated as λ; the angle, θ, at which the beam glances off from the layers of atoms in the fibers; and the distance, d, which separates the layers of atoms. The relationship is expressed by the Bragg formula,

$$\lambda = 2d \sin \theta$$

It is possible to determine the value of λ and θ; therefore the value of d, the distance between the atomic layers, is merely a matter of computation.

When the values of d for a number of sets of atomic layers in the fiber have been determined, it then becomes necessary to obtain the positions of these layers relative to one another. This constitutes the second step.

From this information it is possible to construct a picture of the molecular lattice, from which the elementary cell and the molecular unit of structure are determined.

As the fourth step, a model of the unit of structure is fitted to the lattice; thereupon the picture of the molecular structure of the fiber wall begins to take shape.

The position of the lattice as it occurs in the fiber relative to the long axis of the fiber and to a tangential and a radial orientation in the fiber, will be taken up for consideration as the final step.

DETERMINATION OF ATOMIC LAYERS

The determination of d the distance between atomic layers in the various sets of layers occurring in the fiber, is essentially experimental. The apparatus employed is so constructed that the X-ray beam will have a known wave-length, λ, and that the value of the glancing angle, θ, may be determined.

In its simplest form the apparatus may be represented by the diagram in Fig. 1,

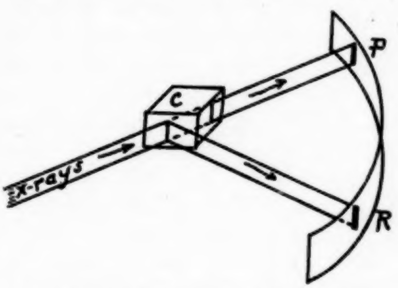


Fig. 1. Perspective Diagram to Show Beam of X-rays Passing Through Crystal, C, to Photographic Film at P; and Beam from Crystal Reflected to the Film at R

where, for convenience of explanation, a simple crystal has been substituted for the fibers at *C*. When a beam of X-rays from a narrow slit is allowed to impinge on the face of the crystal at *C*, the beam is split into two beams; one passes on straight through the crystal to the curved photographic film at *P*, the other is diffracted, or for simplicity of conception let us call it reflected, from the crystal to the film at *R*. Upon development of the film two black lines appear. One was made by the principal beam; the other, by the reflected beam.

The reflected beam is produced only

when the body at C is built up of many layers of atoms. The layers must be parallel to one another and equally spaced. In the figure they are presumed to be parallel also to the face of the crystal. As the beam penetrates the crystal it passes through many of these layers, but not all of it is able to pass, for each layer reflects a small amount, and when the beam impinges on the layers at a certain definite angle these small amounts reinforce one another and produce the line at R.

As mentioned above, a definite relation was shown by Bragg (4) to exist between the *angle* at which the beam impinges on the layers, indicated by θ in Fig. 2; and the *distance* which separates layer from

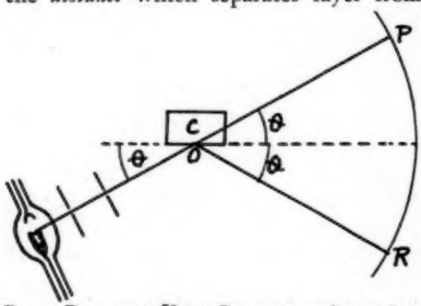


FIG. 2. DIAGRAM TO SHOW RELATION OF ANGLE θ TO THE PRINCIPAL AND REFLECTED BEAMS OF FIG. 1

layer, which was designated as d; and the *wave-length*, λ, of the X-ray waves, such that $\lambda = 2d \sin \theta$. The significance of the two black lines on the film will now become apparent, for from them it is possible to determine the angle θ. In Fig. 2, which is a plan view of Fig. 1, the angle, θ, made by the face of the crystal and the impinging beam is the same as that made by the reflected beam, OR, and also, by the principal beam OP, with the crystal. The distance from P to R on the film then measures the arc of 2θ. By construction of the film holder, O is made the center of the arc PR and the radius of OP is definitely fixed and is a known value. With the arc and the radius known, the value of $\sin \theta$ is merely a matter of computation. Thus one value for the equation above is determined.

The relationship indicated by the equation $\lambda = 2d \sin \theta$, holds only when the X-ray beam consists of waves of a single wave-length; that is, when the beam is monochromatic. It is an easy matter to obtain a beam of this kind, and further, a beam in which the wave-length λ has a known value. This will be discussed later. With λ known, the only unknown in the equation is d, the distance between the planes or layers of atoms; and when d is computed we shall know several things about the body at C. It must have many layers of atoms arranged parallel to one another and all uniformly spaced with the distance between them equal to the value of d as computed from the equation.

If we turn the crystal at C around so that the layers parallel to another face are in reflecting position, the angle, θ, for that face may be found to have a different value, and d, therefore, would also have a different value for this new set of planes or layers. By reflections from other faces the interplanar values of several sets of planes may be determined. If now the angles between these various faces are measured, we shall have the necessary data from which to build a large scale model of the *layers* of the crystal. We cannot build the model from solid planes but if we place blocks at the *intersections* of the planes we shall have a structure in which the planes are all evident, but each plane will consist of a layer of the blocks instead of being a solid layer. This may be seen in Fig. 3 which is a photograph of such a model.

The older theories (9) concerning the structure of a crystal demanded a lattice of elementary particles. We have represented those particles by the blocks in Fig.

3 and the whole structure may be called a three dimensional lattice or, more commonly, a space lattice. The blocks or points of the lattice are known to be identical with atoms or clusters of atoms. The cluster may be a whole molecule, several molecules, or only a part of a molecule. In any case, the distance between the layers is the *d* of the equation.

At this point it may be desirable to consider briefly the quality of the X-ray beam (4) for we are interested here in the use of a monochromatic beam. If the beam as indicated in Figs. 1 and 2 were an

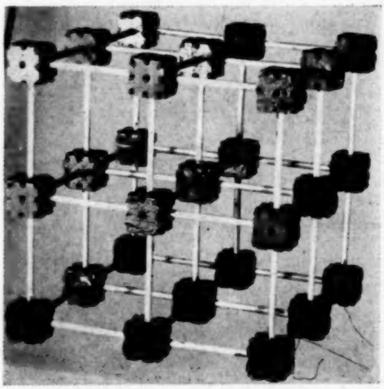


FIG. 3. MODEL OF A SPACE LATTICE WITH BLOCKS AT THE INTERSECTIONS OF THE PLANES

unaltered beam of full strength from an X-ray tube, it would be composed of waves of many different wave-lengths, just as ordinary daylight consists of waves of many sizes. When, in the latter case, the wave-lengths are sorted out by a prism into a spectrum they range in size from about 3900 Å at the violet end to about 7700 Å at the red end. In a somewhat similar manner the wave-lengths of an unaltered X-ray beam, or of "white light" as it is sometimes called, may also be sorted out. These are found to be several thousand times shorter. At one end of the spectrum the wave-lengths may be less than 0.2 Å and at the other end, nearly ten times that length. The distribution of the different wave-lengths in the beam may be nearly uniform, as in ordinary sunlight where no single color or wave-length predominates. This situation exists in the X-ray beam when low voltages are applied to the tube, but when the voltage is stepped up considerably, a single wave-length increases greatly in excess of the others. More specifically, the beam from a molybdenum tube excited at 20,000 volts will have a somewhat uniform distribution of wave-lengths; but, at 40,000 volts, waves of 0.7 Å wave-lengths will occur far in excess of all others; somewhat comparable to a beam of daylight mixed with an intense monochromatic beam such as green light. In both cases it is possible to filter, or screen out, all but the dominating color or wave-length, and thus to obtain a monochromatic beam. In the X-ray beam the predominating wave-length at high voltages is different and characteristic for each element used as a target in the X-ray tube; for tungsten it is 0.21 Å; for molybdenum, 0.71; for copper, 1.54 Å. The exciting voltage differs also for each. To utilize these characteristic wave-lengths practically all others may be screened out by using specific metallic screens; for example, a zirconium filter for a molybdenum target, and one of nickel for the copper radiation.

Returning for a moment to Figs. 1 and 2 and to the equation, $\lambda = 2\,d \sin\theta$, it will be noticed that in the equation, λ refers to a specific wave-length. Obviously then in using an apparatus designed as indicated by the figures, the X-ray beam must be passed through a screen to make it monochromatic. Tubes are readily obtainable with molybdenum, tungsten or with copper anticathodes; and by using the proper screen, λ of the equation becomes a known quantity.

THE RELATIVE POSITIONS OF ATOMIC LAYERS

In practice the procedure is somewhat more complicated than that implied in the description above of work with a single simple crystal, for in biological structures the molecular arrangement is not at all likely to be that of a simple crystal. In the latter the crystal faces are readily seen and the investigator may determine by ordinary crystallographic methods, the faces which are likely to be most advantageous for reflection. But, with biological structures, it is not possible to determine crystal faces by the usual methods;

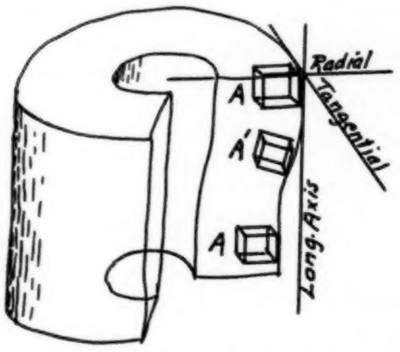


FIG. 4. GREATLY ENLARGED PIECE OF FIBER WITH A SECTOR CUT OUT OF IT
Possible axial lines are indicated

as a rule, they have no faces that have any resemblance whatever to crystal faces. In the case of ramie fibers which we are using here as an example of a biological structure, the fiber is in the form of a cylinder, very slender, perhaps fifty microns in diameter, and very long, often many centimeters in length. The only features of such a structure that even remotely resemble crystallographic axes are the long axis of the fiber, a radius of the cylinder and a line tangential to the surface of the fiber (see Fig. 4).

In order to apply the concepts of the crystal and of X-ray reflection described above, we may imagine a very small cubical piece of the wall, as *A* in Fig. 4, to replace the crystal in Figs. 1 and 2. The front face of that minute block is parallel to the surface of the fiber and the top face represents a transverse plane, across the fiber. Obviously there would be a very large number of these imaginary blocks similarly situated with respect to the surface and to the transverse planes in a fiber; and in order to have an amount of the fiber material sufficiently large, in the path of the beam, to produce reflections to the film a bundle of fibers about 3 mm. thick is required.

Of the hundreds of thousands of such blocks, then, in the path of the beam, a large number would be found to be oriented to exactly the right position to pro-

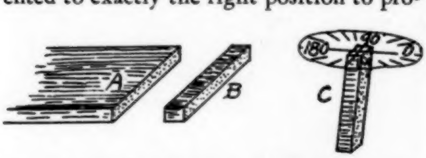


FIG. 5. DIAGRAM TO REPRESENT METHOD OF HOLDING FIBERS FOR X-RAY EXPOSURES

duce a minute reflection from, say, the front face of each; that is, the face which is tangential to the fiber. Another large number would reflect from the side face, that is, a face radial in the fiber; and still another group would reflect from the transverse planes. Such is the case when the fibers are crumpled up and packed into a small 3 mm. pellet. Lines from all three faces of the block would appear at the same time on the film, under those conditions, since each block which was in the proper position for reflection would reflect its small quota to the film, where the summation of all of these small reflections would produce the respective lines. But if the fibers were laid parallel in a bundle, then evidently the *transverse* planes of most of them could be made to form the proper

angle with the beam, all at the same time, and a very strong line would be produced, while practically none of the radial and tangential planes would then be in position to reflect, since the angle θ is a small angle of only a few degrees.

A glance at Fig. 5 may make this somewhat clearer. It represents a convenient device for controlling the position of the fibers. Long fibers were laid parallel and cemented with collodion into a rectangular bundle about 3 mm. thick, 15 mm. wide and of indefinite length, as indicated at *A*. A small piece, *B*, was cut off and attached to a circular protractor as shown at *C*.

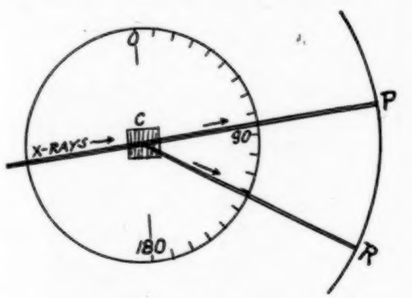


FIG. 6. BLOCK OF FIBERS, ATTACHED TO PROTRACTOR, PLACED IN POSITION FOR X-RAY EXPOSURE

Letters as in Fig. 2. Fibers indicated at nearly right angles to beam.

Thousands of 3 mm. lengths of fibers, of which the piece was composed, would then lie parallel to one another (8), and when the device was placed in the position of the crystal as shown in Fig. 6, it could be rotated so that the beam would pass through at right angles to the long axis of all the fibers in its path. In this position the transverse planes would reflect to *R* on the film, from which, when developed, the distance from *P* to *R* would be a measure of the arc of 2θ for the transverse planes in the fiber.

When this value of θ was used in the formula, $\lambda = 2d \sin \theta$, d was found to be 5.15 Å. From this we are enabled to say that there were many *transverse* planes, or layers, of atoms in the fibers, all spaced 5.15 Å from each other and that these planes were at right angles to the long axis of the fiber. A microtome cross-section of the fiber, one micron thick, might represent a stack of about 2000 of these flat washer-like atomic layers.

If now the protractor is rotated through a quarter of the circle, all of the fibers will lie lengthwise in the beam, along the line 0°–180°, and planes of atoms which extend *lengthwise* of the fiber will be in position to reflect the beam to the film; while the transverse planes will have been turned out of the reflecting position. Here, however, a situation occurs, somewhat different from the preceding and from that in crystals in general, but similar in many respects to the condition found in almost all biological structures, for the cylindrical or curved nature of the material demands special consideration.

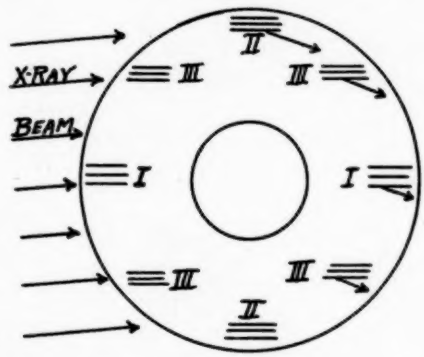


FIG. 7. CROSS SECTION OF FIBER WITH POSITIONS OF REFLECTING PLANES INDICATED I, II, III

When the X-ray beam passes lengthwise through the fiber it finds radial planes, as at I in Fig. 7, and tangential planes as at II, both in reflecting positions, and if those planes have different values for d,

two reflected beams will appear on the film. The photograph taken from that position showed two lines representing planes spaced 6.10 Å and 5.40 Å respectively. We may now say that, in addition to the planes of atoms which extend across the fiber, there are also planes which extend lengthwise. They may be radial and tangential planes respectively, but this is not so conclusive as that the planes considered above are transverse, for if they were in some diagonal position as at III, Fig. 7, they would also produce a reflected line.

The problem, however, is not quite so simple and the whole story has not been told for either of the two positions of the protractor. The photographs obtained from them contained lines other than those mentioned and still more lines were obtained when the protractor was turned to positions lying between 0° and 90°. At the 0° mark a strong line from planes spaced 3.98 Å appeared accompanying the 6.10 and 5.40 lines, as shown in the reproduction of the photograph in Fig. 8. From the 90° position several more lines appeared in addition to the 5.15 line. These are also shown in Fig. 8. When the protractor was turned to the 10° mark, the photograph showed two new lines produced by planes which were not quite parallel to the long axis of the fibers. At the 20° mark other new planes were brought into active reflecting positions; at 30° still more new lines were produced

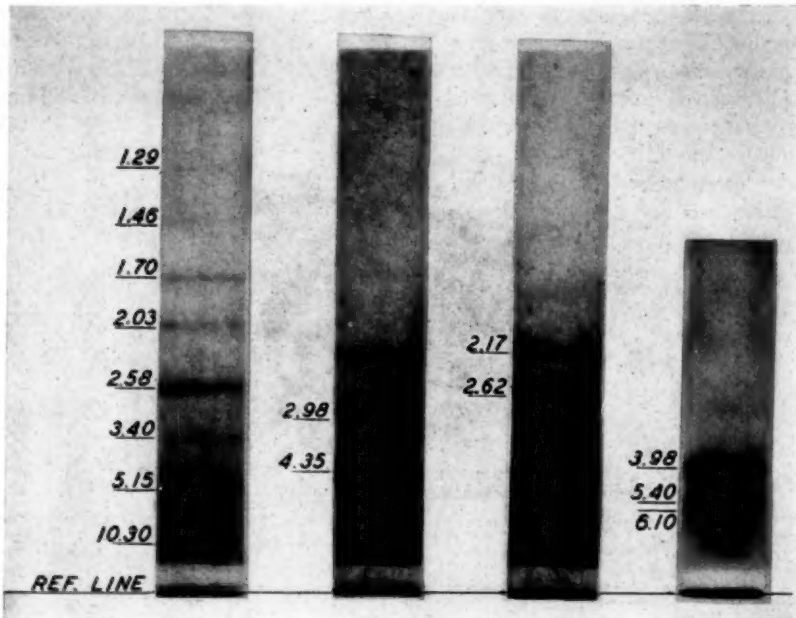


FIG. 8. REPRODUCTION OF PHOTOGRAPHIC FILMS SHOWING THE LINES REFLECTED FROM FIBERS
Position of fibers indicated by 0°, 90°, etc., which refer to protractor readings (see Fig. 6). Interplanar spacings for the lines are given opposite the respective lines.

on the photograph and so on for each ten degree interval to the 90° mark. In all more than thirty lines were found.

THE MOLECULAR LATTICE

Only a few of these lines will be considered here, although all of them must be accounted for in the finally accepted lattice. The former will be used to demonstrate the methods for determining the relative positions, in the lattice, of the planes which produced them; and to show how the molecular structure is deduced from the relation of these planes to one another. In order to help make this clear Fig. 3 is revised, as shown in Fig. 9, to

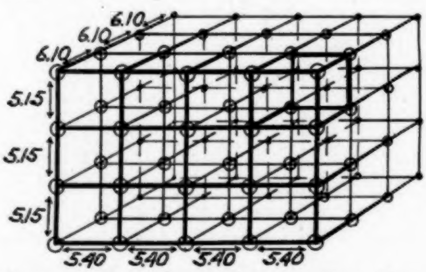


Fig. 9. Diagram of Lattice, Similar to Fig. 3, With the Values in Ångström Units of the Respective Interplanar Spacings for Cellulose Fibers
Spacings computed from lines of Fig. 8

represent one of the minute blocks of cell wall indicated at *A* in Fig. 4. The horizontal layers in Fig. 9 represent the ***transverse*** atomic layers which our photograph from the 90° position of the fibers showed to be spaced 5.15 Å. The layers parallel to the front face of the same block we will assume are spaced 6.10 Å, and those parallel to the sides, 5.40 Å. These two sets of layers we know, from the 0° position photographs, extend *lengthwise* of the fibers. But since we do not know the relation of these two layers or planes to each other, our assumption for the moment is merely a guess.

In the fiber, this minute block (Fig. 9) would appear somewhat as in Fig. 10, where a piece of the fiber is shown in a perspective diagram, but enormously out of proportion relative to the lattice. Another assumption is made here, that the 6.10 Å layers are ***tangential*** and the 5.40 Å layers are ***radial*** in the fiber. The validity of this assumption also will be discussed later. In the figures, the small black circles represent reflecting units of some kind which occur at the intersections of the planes, and of which the planes themselves are composed. These units forming the space lattice in the fiber are spaced 6.10 Å, 5.40 Å, and 5.15 Å respec-

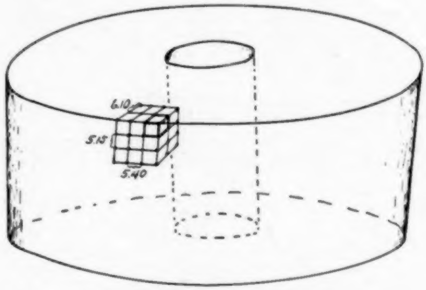


Fig. 10. Diagram of Piece of Fiber to Show Position of Lattice (Fig. 9), in the Fiber
Lattice and fiber greatly out of proportion

tively in the three directions. The lines connecting them are merely for conveniience in guiding the eye to visualize the layers. The lattice, then, may be thought of as composed of cells which are 6.10 x 5.40 x 5.15 Ångströms in size. These are spoken of as the elementary cells of the lattice (3,4). One is shown in Fig. 11 and also one in the near corner of Fig. 9. It is obvious that the elementary cell may be used to represent the whole block of cell wall referred to in Figs, 3, 4, 9 and 10, and that any layers which occur in the block must also occur in the elementary cell. The layers which outline the cell, the faces of the cell, are of

course not the only layers or planes associated with it. Many diagonal planes are distinguishable such as *BCHE*, *DCFE* and *ACGE*, to mention only three of them. Each one represents a great number of planes in the fiber, parallel to it and all uniformly spaced. For example, *BCHE* has a plane parallel to it passing through

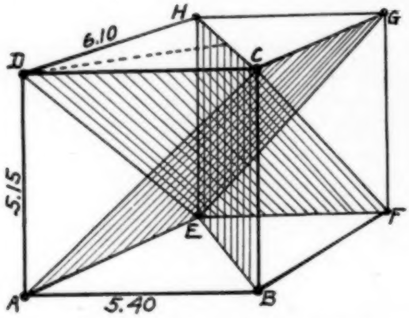


FIG. 11. SINGLE ELEMENTARY CELL OF LATTICE TO SHOW RELATIVE POSITIONS OF VARIOUS PLANES

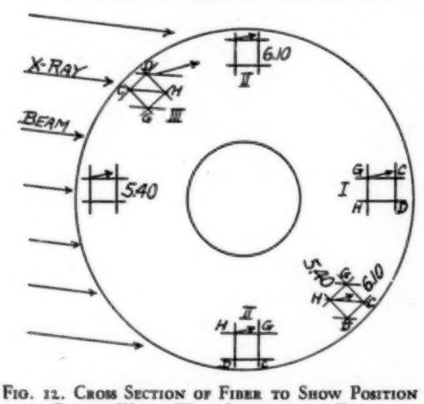


FIG. 12. CROSS SECTION OF FIBER TO SHOW POSITION OF PLANES WHICH WERE INDICATED IN FIG. 11

AD, also another one through *FG*. The *distance*, *d*, between these planes is the perpendicular distance from *D* to the line *CH* (shown by a dotted line), and this distance may be computed since we know that *DC* is 5.40 Å and *DH* is 6.10 Å, provided that we know also the angle between those two sets of planes. Further, when we look back to Fig. 7 and revise it as in Fig. 12, where only the top layer of the elementary cell is shown at the positions of I, II, and III of Fig. 7, it may be seen that at I, in Fig. 12, the planes which are spaced 5.40 Å will be in position to reflect the beam; at II, the 6.10 planes will reflect, and at III the *diagonal* plane which passes through *CH* of the cell should also reflect the beam. We might expect then to find on the photograph which shows the 5.40 and 6.10 lines, another line from planes which are spaced a distance equal to the dotted line from *D* to *CH* in Fig. 11. On the photograph in Fig. 8, 0° position,

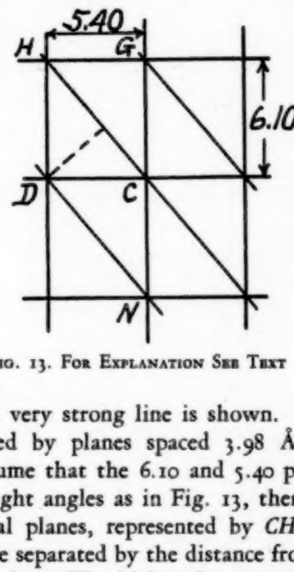


FIG. 13. FOR EXPLANATION SEE TEXT

a third very strong line is shown. It is produced by planes spaced 3.98 Å. If we assume that the 6.10 and 5.40 planes form right angles as in Fig. 13, then the diagonal planes, represented by *CH* and *DN*, are separated by the distance from *D* to the plane *CH* which, when computed, is found to be about 4.05 Å. The experimentally determined 3.98 is close enough to the theoretical value 4.05 to serve as a first approximation. Therefore, for the moment, we may accept the elementary cell as being an orthorhombic structure (3); that is, one in which the angles between the faces are right angles. This is a tentative working hypothesis which

will be checked by other diagonals and modified to fit them, since the structure which is finally accepted must have planes corresponding to all of the lines found on the photographs.

The set of diagonal planes with the interplanar spacing of 3.98 Å produced an exceptionally strong line; that is, strong relatively to the 6.10 and 5.40 lines. This indicates that the atoms associated with the corners *B*, *C*, *H*, and *E* of Fig. 11 are located in positions which are more efficient as a group in reflecting from the diagonal planes, as represented by *BCHE*, than from the face planes of the cell; that is, from the 6.10 and 5.40 planes. The question then arises, what atoms or molecules may we expect to find at these corners?

THE MOLECULAR UNIT

The chemist assures us that cellulose consists of only three kinds of atoms: carbon, hydrogen and oxygen. A conception of the elementary cell with only one atom at each corner is not consistent either with the intensities of the lines on the X-ray photographs or with the sizes of the atoms (3), which incidentally have radii of less than one-fourth the distance from corner to corner of the cell. It seems more reasonable then to think that a *group* rather than a single atom occurs at each corner. The most obvious group for consideration is that composed of six carbon, ten hydrogen and five oxygen atoms, ($C_6H_{10}O_5$), since it contains, in simplest numbers, the proportion of each of the elements, in cellulose. If this group, which is called a glucose residue, occupies a space equivalent to the volume of the elementary cell or bears some integral relation to it, there would be a high degree of probability that the group is the structural unit.

The volume of the $C_6H_{10}O_5$ group may be computed from data which are in no way associated with the X-ray data from cellulose. It is known that there are 6.062×10^{23} molecules in a gram-molecule of a substance. In the case of cellulose the $C_6H_{10}O_5$ group may be accepted as the molecule for this purpose. Its molecular weight is 162. The gram-molecule, 162 grams, then contains 6.062×10^{23} glucose groups. The volume of 162 grams of cellulose is 103.2 cubic centimeters since the specific gravity is 1.57; that is, one cubic centimeter weighs 1.57 grams. If then 6.062×10^{23} groups occupy a volume of 103.2 cubic centimeters, the volume of

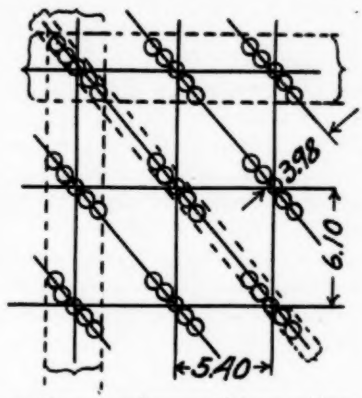


FIG. 14. DIAGRAM TO INDICATE MOLECULAR GROUPS IN THE LATTICE AND MOLECULAR LAYERS OR PLANES

one group is $103.2 \div 6.062 \times 10^{23}$ which is 170×10^{-24} cc. or 170 cubic Ångströms. Returning now to our tentative elementary cell, we find its volume $6.10 \times 5.40 \times 5.15$ to be 169 cubic Ångströms. The agreement between these two volumes, elementary cell 169, glucose residue group 170, makes it seem very probable that the group of atoms located at the corner of the elementary cell is identical with the $C_6H_{10}O_5$ group of the chemist.

Attention was called to the exceptionally strong 3.98 line in Fig. 8. The significance of this becomes clearer now when we revise Fig. 13 by placing $C_6H_{10}O_5$

groups at the corners of the cells in Fig. 14. When they are so placed that most of the atoms lie along the diagonal planes and close to it, they form a relatively thin layer of atoms from which the 3.98 lines are produced; while at the same time in the direction of the 6.10 and 5.40 planes they form thick layers as indicated by the dotted lines. Since all of the atoms of a given set of layers are effective in reflection, the intensity of the line produced is in this case dependent to a great extent upon the thickness of the individual layers in some inverse ratio (3). The arrangement of the atoms in the group seems to fit, at least qualitatively, the density of the lines shown in Fig. 8. For a more complete demonstration of this the literature (10) may be consulted.

A molecular picture of the fiber is now beginning to be unfolded. Figure 14 might represent a view of the molecular arrangement on a cross-section of the fiber. It is quite impracticable to draw a complete cross-section of a fiber to scale and show the molecular arrangement, for if the layers of molecules were represented by circles only $\frac{1}{8}$ inch in diameter, it would require a circle 400 feet in diameter to represent the fiber cross-section. Referring again to fig. 14, we have shown up to this point, that if we could magnify a *cross-section* of a fiber sufficiently and could attune our eyes to see individual molecules we would perceive an orderly arrangement as in the figure, with the distances from center to center as indicated, and the molecules would appear longer along one diagonal than in any other direction.

We now turn to the appearance of the groups as seen on a tangential or radial section of the fiber; and elect, as a convenient angle at which to view them, to look along a line such as the dotted line in Fig. 13 from *D* to *CH*. This will give a broadside view of the $C_6H_{10}O_5$ group. When the fiber block of Figs. 5 and 6 was rotated to the 90° position several lines (Fig. 8) from transverse planes in the fiber were produced in addition to the 5.15 line which was used in the tentative elementary cell. These additional lines indicate the presence of *several sets* of atomic planes *all* parallel to one another and *all* at right angles to the long axis of the fiber. The interplanar spacings corresponding to the more prominent lines are 5.15 Å; 3.40; 2.58; 1.70; 1.29. If a small sub-group of atoms existed half-way between the 5.15 planes,

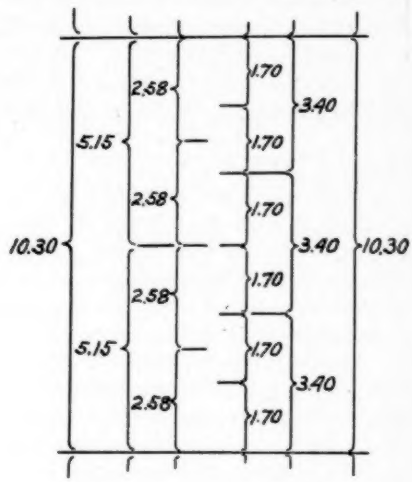


Fig. 15. For Explanation See Text

it would account for the 2.58 line; and if another sub-group interleaved the 2.58 planes, the 1.29 line would be explained; but 3.40 does not seem to bear a multiple relation to 5.15. If, however, we were to consider *two* of the glucose groups as forming *one* structural unit, the total length of which is 2 x 5.15 = 10.30 then all of the lines would be accounted for. This double unit, 10.30 Å long, repeated lengthwise of the fiber, may be more clearly understood from Fig. 15, where the multiple relation between the various planes is brought out.

The combined effect of reflections from all of the atoms within each 10.30 distance produces a resultant line on the photographic film; the resultant for all within the 5.15 distances produces another line; for all within 2.58 distances still another line, and so on. It would seem then that with these interleaved groups spaced so closely together, the glucose *units* would not appear to be so distinctly separated in the lengthwise direction of the fiber, as they are in the transverse view. They would have the appearance of chain-like structures extending lengthwise of the fiber parallel to one another with the chains spaced 6.10 Å in one direction and 5.40 Å in another (11). The groups in Fig. 14 would represent the end view of these chains as seen on the transverse section of the fiber.

Up to this point, we have considered only the lines which were produced by transverse layers and by layers which extend lengthwise of the fiber. These lines were obtained from exposures with the fibers in the 90° and 0° positions respectively (Fig. 8). The remaining twenty odd lines represent diagonal layers and were produced by rotating the fibers to positions between 0° and 90°. In the geometrical figure which was finally accepted as representing the lattice, diagonal planes were found which corresponded to all of these lines.

Returning again to a consideration of the individual chain, we must now think of every 10.30 Å length of it as being exactly like the next adjoining 10.30 Å length along the chain; and of the unit of structure along the chain as consisting of two $C_6H_{10}O_5$ groups, each 5.15 Å long. In order to explain the 10.30 and 3.40 lines on the film, we must suppose one of the two groups to be oriented slightly differently from the other; the chain then consisting of a single row of $C_6H_{10}O_5$ groups, with the alternate groups alike in orientation.

The elementary cell must now be revised to include this new conception of two groups forming the unit distance along the chain. The revision merely makes two of our former elementary cells into one twice as long; that is, 6.10 x 5.40 x 10.30. But when we examine the reflection lines obtained from the block of fibers at positions between 0° and 90° (Fig. 5), we find that in order to explain the occurrence and intensities of some of them we must alter again the dimensions of the elementary cell. This time it is due to a difference in orientation of one *whole chain*

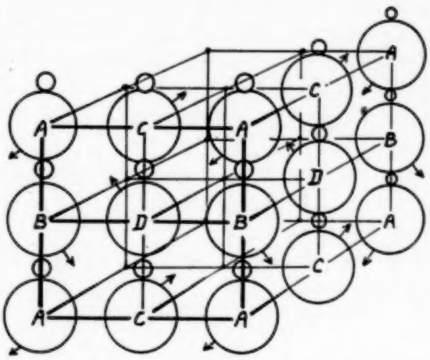


FIG. 16. DIAGRAM TO SHOW MOLECULE OF THE LATTICE ORIENTED TO FOUR DIFFERENT POSITIONS, INDICATED BY A, B, C, AND D

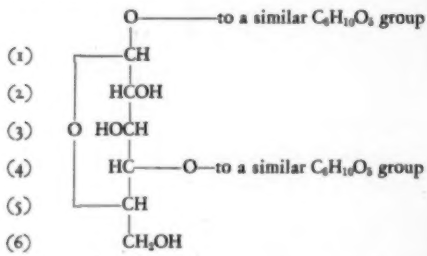
Large circles represent the glucose residue; the small circles, the oxygen bridges. Arrows merely indicate different orientations.

from that of the next adjacent chain; thus *alternate chains* in the 6.10 and 5.40 layers are so rotated on their long axis that the alternate *chains* have like orientation, otherwise all of the chains are alike. This construction, with the chain consisting of a single row of $C_6H_{10}O_5$ groups, all alike chemically, but with only the alternate ones oriented alike in the chain, and the *chains* also all alike except that only the alternate chains have like orientation, accounts for all of the thirty-odd lines obtained in the X-ray diffraction patterns. In Fig. 16 a diagram of this

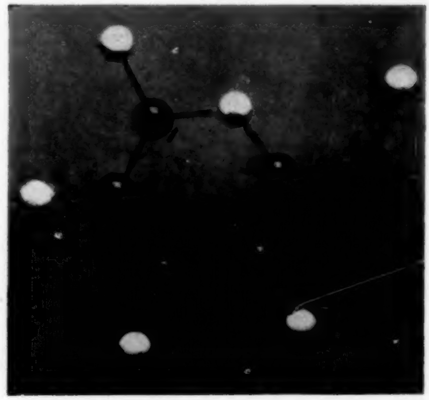
arrangement is given. The large circles which represent whole $C_6H_{10}O_5$ groups now replace the black dots of Figs. 3 and 9. In the latter case the dots represented merely the centers of some kind of reflecting units, now we may substitute a $C_6H_{10}O_5$ group for each reflecting unit. The letters, *A, B, C,* and *D,* in the figure, are used to indicate the difference in orientation of the glucose groups. Those of a given letter have like orientation. The arrows are used merely to help that conception.

ATOMIC MODEL OF THE UNIT OF STRUCTURE

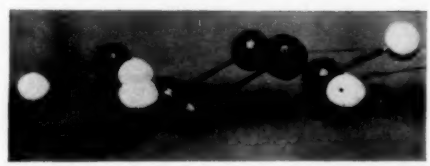
The chemist, through his experimental methods, gives us the relation of the atoms to one another in the molecule and indicates the structure of cellulose somewhat like this:



When, however, we use the physicist's dimensions of the atoms concerned (3), the picture of the group becomes a three-dimensional structure of a very different shape. The four valence bonds of the carbon atom are localized at tetrahedral positions on each atom; that is, at positions which would correspond to alternate corners of a cube, about 109° apart (12). The two bonds of the oxygen atom are also at tetrahedral points (13). The distances from center to center of the atoms are generally accepted as about 1.50 Å, carbon to carbon; and 1.40 Å, carbon to oxygen. The hydrogen atoms may be ignored since their contribution to X-ray reflection here is not measurable. In constructing a model, however, the diameter was considered to be roughly about 1 Å. A photograph of a three-dimensional model using these dimensions and angles is shown in Fig. 17 a and b. When carbon 1 is attached through an oxygen atom to carbon 5, a ring structure is formed which



A



B

FIG. 17. REPRODUCTION OF A THREE-DIMENSIONAL MODEL OF A GLUCOSE MOLECULE; A, FLAT VIEW, B, EDGE VIEW

Black spheres represent carbon atoms; white, oxygen. Hydrogen atoms are not shown.

turns out to be 5.15 Å long; that is, from the oxygen atom of carbon 1 to the oxygen atom of carbon 4. According to the chemist, these two oxygen atoms act as bridges which link the glucose residues or groups together by primary valence forces into long chains; and when the adjacent residues are oriented slightly differently, but

with the alternate ones all alike, the structure is in agreement with the elementary cell constructed from the X-ray diffraction patterns (10, 14). It is interesting to note that, at the same time this lattice model was being worked out by the author from X-ray data, chemical evidence was presented independently for the same ring structure (15), and for the same oxygen bridge as was used in the arrangement of residues in the chain.

In Fig. 18 the relation is shown between the various sets of planes and the atoms in the model. In our first attempt at fitting

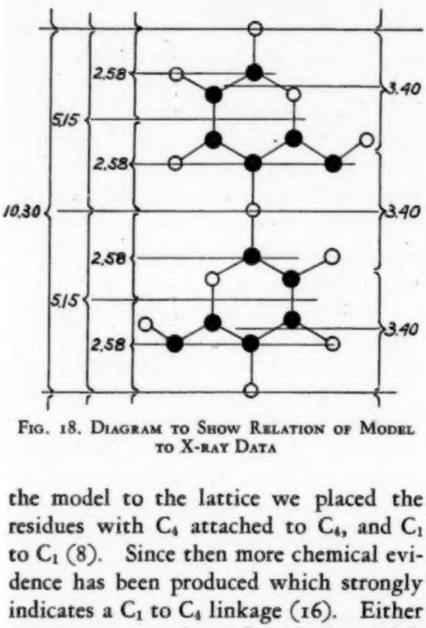


FIG. 18. DIAGRAM TO SHOW RELATION OF MODEL TO X-RAY DATA

the model to the lattice we placed the residues with C_4 attached to C_4, and C_1 to C_1 (8). Since then more chemical evidence has been produced which strongly indicates a C_1 to C_4 linkage (16). Either arrangement may be made to fit the model, but a discussion of this point is of little importance at the present time to the biologist. Another phase of orientation is, however, of more direct interest; that is, the position not merely of one of the units or one of the chains, but of the *whole lattice* as it occurs in the wall with respect to the fiber as a whole.

POSITION OF LATTICE IN FIBER

In Fig. 14, where the end view of the chains is shown, they are indicated as being flattened along one of the diagonals. The model fits very well into this arrangement both in shape and in dimensions. But whether the *lattice* is so arranged that a certain set of planes is always tangential to the surface of the fiber, as we have tentatively assumed in Figs. 10 and 12, or whether it has some other arrangement, does not appear from the data presented up to this point. In a cylindrical structure such as a fiber, the different sets of planes which lie parallel to the long axis, will be found to lie all at the same time, in a position favorable for reflection somewhere in the fiber, as shown by Fig. 7. There seems to be no way of determining

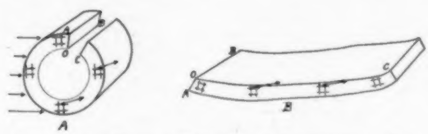


FIG. 19. A, PIECE OF FIBER SPLIT LENGTHWISE; B, SAME PIECE FLATTENED OUT, TO SHOW POSITION OF LATTICE

directly their position with respect to one another, or to the surface of the cylinder; but if the cylinder could be split lengthwise and flattened out as indicated in Fig. 19 then each set of planes could be brought into reflecting position independently of the others, and then by rotating through known angles, the relative positions could be determined. Obviously, however, the fibers are too small to be split, and besides, some thousands would have to be piled up into a block, in order to have enough material to produce a diffraction pattern. In searching for other material which could be used in this way, the large cells of a seaweed, *Valonia*, were found to be satisfactory (17, 18). They are spherical cells 10 to 20 mm. in diameter. Pieces

about 3 mm. square were built up into a layered block and cemented with collodion. When this block was placed in the cassette, as at *C* in Fig. 2, and rotated to bring the tangential planes into reflecting position, the 6.10 line was strongly produced (see Fig. 20), showing quite conclusively that the 6.10 planes were placed tangentially in the wall. When rotated approximately 90° from that position, a 5.33 line appeared on the film, and at the 45° position a 3.93 line. These two correspond to the 5.40 and 3.98 lines respectively from the fibers. The angle between the 6.10 and 5.33 planes was 88°, instead of being exactly a right angle. This may be accepted as direct evidence that the arrangement of the planes is as shown in Fig. 14. It seems reasonable from several points of view to accept the flat piece of *Valonia* as comparable to a split fiber flattened out as represented in Fig. 19, and to carry over this conception of the lattice to the cell wall in general, in which we may say that the tangential planes are spaced 6.10 Å apart and the radial, 5.40 Å.

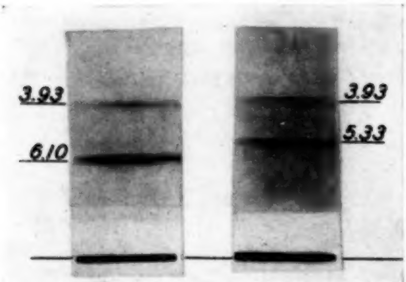


Fig. 20. Diffraction Lines from Valonia Cell Wall

SUMMARY OF CELLULOSE STRUCTURE

Perhaps the attempt in the preceding pages to develop the molecular structure of cellulose step by step, has been obscured by the inclusion of too many details. If that is so, then a brief summary may prove useful, especially since the methods are, in general, those which are likely to be used for similar work with other biological structures.

The existence of parallel layers of atoms uniformly spaced in the cell wall follows from the fact that fibers produce X-ray diffraction patterns.

The positions of these layers in the fiber were determined, in part, by placing the fibers so that only specific sets of layers would be properly oriented to produce diffraction lines. Three sets were shown to extend lengthwise of the fiber, and several additional sets, transversely in the fiber at right angles to the former.

When these planes were graphically built into a geometrical three-dimensional structure or lattice, using the interplanar spacing values which were determined from the lines, it was found that the structure would account for all of the additional lines obtained from other positions of the fibers.

The molecular unit, indicated by the lattice thus formed, was found to have a volume equal to that of the glucose residue ($C_6H_{10}O_5$) which is ascribed to cellulose by the chemist.

In order to account for the intensity of some of the lines, and for the presence of certain others on the photographic films, it seemed necessary to assume that only the alternate residues must have like orientation.

The elementary cell, that is, the structure which, when repeated, would produce the lattice, would then consist of four glucose residues all differently oriented.

The several sets of transverse planes, all of which fitted into a 10.30 Å distance, the length of the elementary cell, led to the idea of a chain formation of the residues along the long axis of the fiber, each residue being 5.15 Å long.

From the chemical evidence, and from the attempt to fit a model of glucose units into the lattice, it was found that the most acceptable arrangement consisted of chains of glucose residues linked together through oxygen atoms.

Work with the alga, *Valonia*, brought out the facts that the layers which were tangential to the surface of the cell were spaced 6.10 Å; the radial, 5.33 Å; and further that the angle between these two planes was almost a right angle, more exactly, 88°.

Very briefly then, the cellulose wall of fibers consists of glucose residues linked together into long chains which extend lengthwise of the fiber, parallel and uniformly spaced; with the tangential layers of chains spaced 6.10 Å, the radial layers, 5.40 Å and in the chain itself the residues spaced 5.15 Å from center to center.

VALIDITY OF CELLULOSE STRUCTURE

The conclusions given above were based, as previously mentioned, upon data and concepts taken from several apparently remote fields of science. Under such circumstances one is likely to wonder how valid they may be. In working with inorganic crystals, X-ray analysis calls upon chemistry merely to learn what kind of atoms are present in the crystal and how many of each there are in the molecule. With that information at hand, the analysis may proceed from X-ray data alone to consideration of a complete atomic structure of the crystal. As a check upon the correctness of the view of the structure, the theory of space groups as applied to crystals (3, 9) has become a part of the analytical procedure, and the structure determined from experimental evidence must be in agreement with the theory.

When working with organic crystals, however, such as those of the carbohydrates, amino acids and others, chemistry is called upon not only for the determination of the kind of atoms, and for the number in the molecule, but also to give the relative positions of these atoms in the molecule. The use of the space group here becomes limited to the location of the molecule as a whole, instead of using it to check the positions of the individual atoms, as in the case of inorganic crystals; for in the organic crystal the *molecule* as a whole acts as the unit of the lattice, whereas in the inorganic crystal the *atom* acts as the unit. There are, of course, exceptions to these statements, but here the attempt is made to give merely a general picture of the situation.

Biological structures, such as those in which we are especially interested for the moment, are not at all likely to have their molecules and atoms as nicely arranged as they are in the more characteristic crystals where faces and axes are determinable by crystallographic methods. In structures produced by organisms forces are active in their formation which are not present in solutions when ordinary crystals are deposited (19). The presence of these additional forces in living protoplasm prevents a clean cut regularity in arrangement of the molecules; that is, it introduces irregular arrangements, or a degree of amorphousness. The effect of this irregularity upon the X-ray diffraction pattern is indicated by a blurring and spreading of the lines, and by a diffuse darkening of the spaces between the lines on the photographic negative. As a result, in studying such structures the analysis becomes less certain; and chemistry is called upon for all the information it can give. It is probable, as mentioned above, that included in the forces involved in the deposition of materials by the protoplasmic matrix, there are others in addition to those of crystallization. If this is the case, then the determination of the space

group for a given organized substance will have little value.

It seems doubtful whether any structure of plant or animal origin will be found, which will yield to structural analysis with the same degree of assurance of accuracy that is possible with inorganic crystals, or even with organic crystals. In any case the fine structure of a material should offer a reasonable explanation for many *properties* of that material; and whenever an exact determination cannot be arrived at with the certainty that is obtained for many inorganic crystals, the relation of the structure to its properties is a reasonable source of information upon which to draw. For example, in the studies on cellulose the molecular lattice was worked out with only one assumption of a chemical nature. That assumption was that the molecular unit is identical with the glucose residue which is obtained from cellulose upon degradation by hydrolysis. But, in order to fit this residue into the lattice, it was necessary to turn to carbohydrate chemistry for the basic evidence bearing on the positions of the atoms in the glucose molecule (10). That evidence showed that the residues were linked through an oxygen bridge, while the X-ray data pointed to the long chain, with the residues forming links of the chain. Additional chemical evidence has lately been presented (20) to support this conception of chains of indefinite length. To the same end, investigations by X-rays on many derivative products of cellulose (21) have shown that the 5.15 Å distance, which is the length of the residue, remains as predicted (10), wherever the fibers are not broken down in the process. From another point of view, physical properties of the fiber are in agreement with the chain structure. The coefficients of thermal expansion (22) indicate that lateral vibration is greater than longitudinal; and swelling experiments (23) show that the chains separate laterally, while no extension longitudinally takes place. Both are in accord with the lattice proposed, where primary valence forces hold the units into the chain more strongly than the forces known as van der Waals' forces hold the chains together laterally.

The development of the glucose-residue chain conception of the structure of cellulose was the outgrowth of a number of investigations covering a period of nearly two decades. As the work progressed, the methods and technique changed somewhat, resulting in greater accuracy in determination of the lattice. In 1913, shortly after the discovery of the use of crystals as diffraction gratings for X-rays, two Japanese investigators reported (24) X-ray evidence of molecular uniformity in the structure of fibrous materials. After an interval of seven or eight years, several reports appeared in German periodicals (25), in which the dimensions of the elementary cell of a lattice were given, but the data were insufficient for a detailed picture of the cellulose structure. A few years later, 1925–1926, three articles (8, 10, 11) appeared in American journals embodying the essentials of the structure as described in the present paper. In 1928 several German investigators (16) verified this structure with only a slight alteration, that of the orientation of the alternate glucose residues in the chain. This change was made in order to bring the structure into better agreement with chemical evidence which was then available. Since then X-ray work with cellulose has dealt mainly with its properties, and with its derivatives. The measurements of a dozen or more derivatives in which the fiber retained its gross structure, show that the 5.15 Å unit distance, the length of the glucose residue, is retained throughout (21).

The methods of crystal analysis have

been improved somewhat during the past decade, although the fundamental principles have remained the same. Two of these modifications may be of especial interest to the biologist; the first is a method of *obtaining the reflections* of X-rays from the materials, the second is a means of *determining the reflecting planes* of the lattice. Concerning the former, instead of using a slit to control the X-ray beam, a minute round hole is used. The beam from this pin-hole is allowed to pass through the material under investigation and the reflected beams are recorded on a photographic plate. Practically all of the planes are brought into reflecting position, during one exposure of the plate, by rotation of the crystal or the material (3). Fig. 21 is a reproduction of such an exposure of cellulose fibers. Each spot is the result of reflection from a specific set of atomic planes.

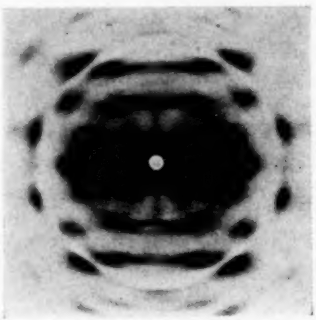


Fig. 21. Diffraction Pattern From Cellulose Fibers Taken With Pin-hole Beam of X-rays (From Astbury)

A simple means of determining the planes, in crystallographic terms, from these spots was devised (26) in the form of a chart. Fig. 27 is an example of the use of the chart, where the spots from X-ray patterns of hair and wool have been transferred directly from the photographic films. The reflecting planes for each spot may be read directly from the chart and in most cases a far greater degree of certainty is obtained than was possible with the method described above. For details of the later method the reader is referred to the original report and to Wyckoff's "Structure of Crystals," New York, 1931 edition.

OTHER BIOLOGICAL STRUCTURES

As has been mentioned in the early part of this article, a dozen or more biological materials and structures in addition to those of cellulose have been studied by X-ray methods. Only a few of these have so far yielded results which may be considered as even moderately satisfactory for the interpretation of molecular structure. Numerous investigations of carbon compounds brought to light several outstanding points which are of especial interest to the biologist, since they are sufficiently fundamental to be applicable to studies of organized materials in general.

Through the work of several investigators (27) it has been shown that in the fatty acids the long hydrocarbon chain is a zig-zag structure. It corresponds to a structure built up of carbon atoms having diameters of 1.5 Å attached to each other at tetrahedral angles (109°), and as increasingly higher forms were studied, it was shown that the length is increased by a specific distance for each —CH_2— group added to the chain. The distance is slightly less than 1.3 Å, which is in good agreement with corresponding distances between the carbon atoms of the diamond (12). With this work in mind one feels greater confidence in accepting a similar zig-zag arrangement for the carbon atoms in the carbohydrates, and in fact, in the carbon compounds generally.

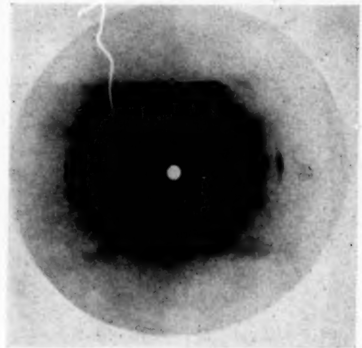
A great deal of emphasis has been placed upon the idea that organized substances are composed of long chain molecules (14).

To most of these substances, as will be seen in the following brief accounts, there has been assigned a molecular structure based primarily on analogy to cellulose either from the similarity of X-ray diagrams or from the similarity of chemical and physical properties. For none of these substances has there been as complete an X-ray analysis as for cellulose. In many cases such completeness may not be possible, but in others more concentrated work may give as good or better results.

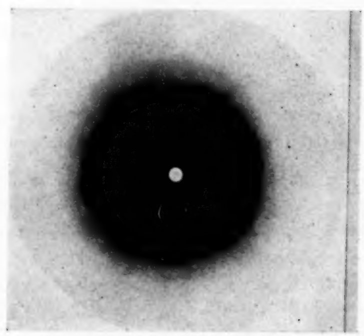
There seems also to be a general assumption arising from the work on fiber structure, that "fibers are fibers, because their molecular components are fibrous;" and structures have been proposed upon that basis when sufficient X-ray data were not available for the purpose.

Rubber

When raw rubber is in a stretched condition, an X-ray pattern may be obtained from it; but when the rubber is in an unstretched condition the photograph is similar to that obtained from amorphous materials. The pattern from the former was interpreted as indicating the existence of long chain molecules in which isoprene groups are the units, somewhat as glucose groups are units in the cellulose chain. Isoprene (C_5H_8), from its formula, might be considered comparable to the hydrocarbon chain of the fatty acids in so far as the atomic arrangement in its molecule is concerned. This possibility was taken into consideration apparently, when the structure of rubber was proposed (14), for the X-ray pattern, Fig. 22, contains only a few lines. These lines alone were insufficient for the determination of the lattice, but with the help of data from chemical sources and from various other sources in which the physical properties of the rubber were concerned, the lattice was worked out. The two types of photographs obtained were interpreted as indicating that the stretching and the contraction of rubber were associated with a corresponding straightening out and wrinkling of the long chain molecules.



A



B

FIG. 22. X-RAY PATTERNS FROM RUBBER; A, WHEN STRETCHED TO SEVEN TIMES ITS ORIGINAL LENGTH; B, UNSTRETCHED
(From Astbury)

Carbohydrates

In a somewhat similar manner, conceptions of the structures of several carbohydrates have been proposed, which were based to a great extent upon the chemical formulae, and only partially upon X-ray data supplemented by physical properties, and strengthened by analogy to the structure of cellulose. Among these are starch,

lignin and hemicelluloses, tunicin and chitin, and others. From none of these substances has an X-ray pattern been obtained which is sufficiently clear and which has enough detail to justify more than a tentative structure. Since most of the reports on carbohydrate investigations have been collected in a late publication in book form (14), we shall describe here only very briefly the molecular structures which have been proposed for them.

Hemicelluloses, such as occur in date seeds and the fruits of several palms, produce sharp X-ray patterns, but up to the present time no clear cut demonstration of the lattice has been offered. A chain structure has been proposed (14), in which hexose residues act as the units; however, it is based primarily upon chemical considerations.

Concerning lignin practically nothing has been determined by X-ray means, but from chemical considerations, again, a primary valence chain comparable to that in cellulose is thought to represent the structure (14).

The crystalline nature of the starch grain has been debated for nearly a century; but it was not until 1920, when X-ray diffraction patterns were reported (25), that the existence of a crystalline regularity of its atoms was definitely demonstrated. A few years later the molecular unit of structure was shown, with a fair degree of probability, to be a glucose residue (6). Soon after that, evidence was presented which made it seem probable that the arrangement of the units in the starch grain was not the same for grains from different kinds of plants (35). The structure has not yet been satisfactorily worked out, although from its chemical and various physical properties a chain structure similar to that of cellulose was proposed (14) in which glucose residues are the links of the chain.

The so-called animal cellulose, tunicin, which forms the framework of the tunicates is capable of producing a moderately good X-ray pattern, sufficiently good it was thought (14) to consider it as indicating a molecular chain structure identical with that of plant cellulose. Curiously its diffraction pattern is quite like the pattern which may be obtained from the alga *Valonia* in that its 6.08 Å and 5.45 Å planes correspond to the 6.10 Å and 5.33 Å planes respectively of the latter, and also in that the angles formed by these

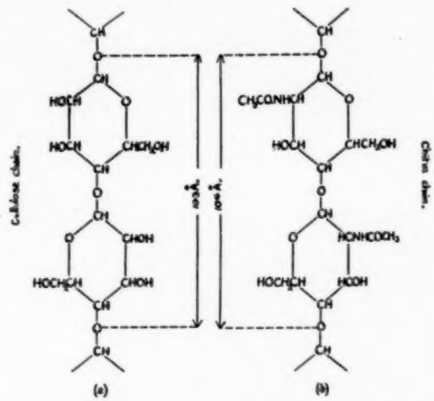


FIG. 23. DIAGRAM TO SHOW RELATION OF CHAIN MOLECULE OF CELLULOSE TO THAT OF CHITIN

planes are the same. Its diagonal, spaced 3.95 Å corresponds to the 3.93 Å of *Valonia* (28). That an animal such as a tunicate is capable of forming cellulose is in itself interesting, but that the cellulose is deposited in the same molecular arrangement as that in the plant cell wall is remarkable, and may have a special significance when the methods of deposition are more fully studied.

Chitin, as represented by the wing covers of the Goliath beetle, gave an X-ray pattern from which a repetition period of 10.4 Å was obtained (14). The similarity to the 10.3 period of cellulose led to a

proposed chain structure in which acetylglucoseamine residues with a ring structure almost identical with that of cellulose, acted as the links of the chain. Fig. 23 shows the similarity between molecules of the two substances. The principal difference is in the addition of an NHR group to carbon number two of the glucose residue. The evidence for this is entirely of a chemical nature.

Proteins

Of all structures built by organisms, those composed of proteins are undoubtedly of the greatest interest to the biologist; they are also the most elusive, as becomes obvious when one attempts to gain a conception of their structure. The large size and the great complexity of protein molecules make an understanding of their structure seem exceptionally difficult, if not hopelessly impossible to attain. The relation of amino acids to the proteins offers a certain amount of hope, however, and X-ray studies on silk, wool, hair and other proteinaceous fibers add further encouragement. In 1921, and also a year or so later, it was reported that such fibers (29) were capable of producing X-ray diffraction patterns which were similar to those of cellulose fibers, although less complete and less well defined.

In 1923, the idea was advanced (30) that silk-fibroin consisted, to a considerable extent, of primary valence chains arranged parallel in the direction of the fiber. The similarity of the X-ray pattern, Fig. 24, to that of cellulose, Fig. 21, indicated a long chain structure in the silk also. The elementary cell which was proposed showed that the chains were spaced 4.40 Å and 4.84 Å laterally at nearly right angles, while along the chain the repetition distance was given as 7.0 Å. It is this last dimension which is of especial importance in connection with proteins in general, for the conception was advanced that the chain consisted of peptide linkage units with the residues of the amino acids attached as side chains. In the silk fibroin the amino acids involved are principally glycine and alanine. When they are built

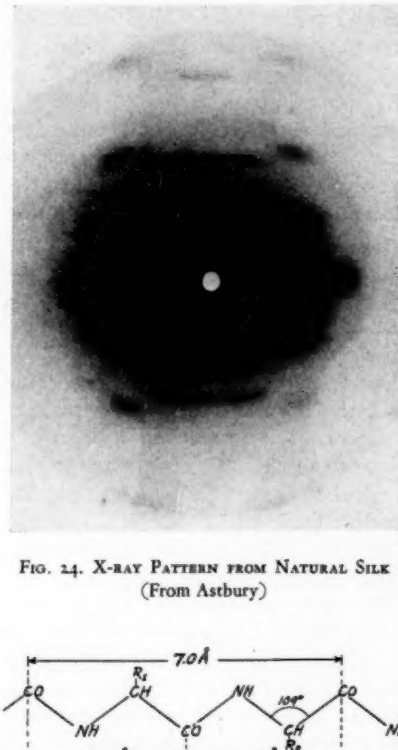


Fig. 24. X-ray Pattern from Natural Silk (From Astbury)

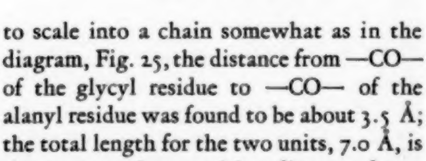


Fig. 25. Diagram to Show Relation of Peptide Linkages to X-ray Spacings from Silk (From Astbury)

to scale into a chain somewhat as in the diagram, Fig. 25, the distance from —CO— of the glycyl residue to —CO— of the alanyl residue was found to be about 3.5 Å; the total length for the two units, 7.0 Å, is the same as the repetition distance determined from the X-ray pattern of the silk fiber. A diagram of the model is shown

in Fig. 26. The structure is one which seems to be in harmony with various physical properties of the silk fibers, and may be considered as the most satisfactory one proposed up to the present time. A significant feature of it is that it provides a way for placing amino acids which vary in size into a chain, in which the links have a uniform length of about 3.5 Å along the fiber axis. The remaining part of the amino acid residue then becomes effective in governing the distance to which the chains may be separated. Another correlation which is of interest here

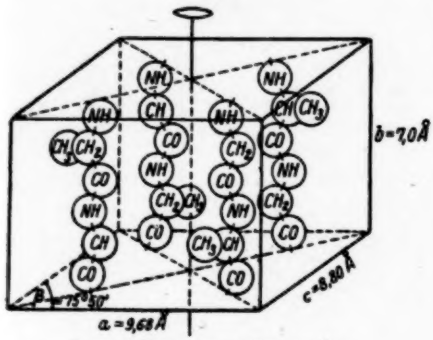
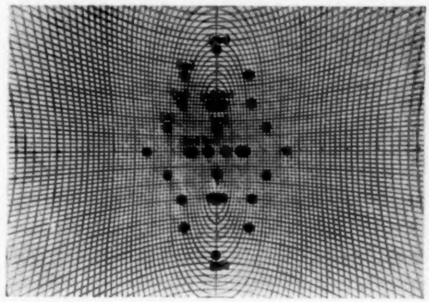


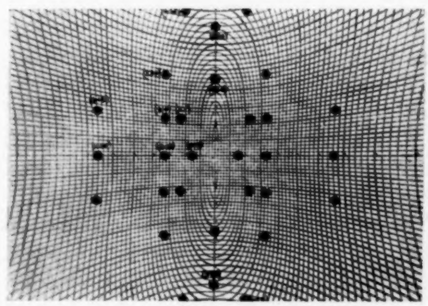
FIG. 26. ELEMENTARY CELL OF SILK
(From Meyer and Mark)

is that the distance between four $—CH_2—$ groups in the fatty acid chain mentioned above, $—CH_2—CH_2—CH_2—CH_2—$, is practically the same, 3.7 Å, as that from one —CO— group to the next —CO— group, —CO—NH—CH—CO, of the peptide chain, 3.5 Å. The similarity in dimensions is at least striking.

A more marked advance was made on protein structure in 1930 when a group of investigators (31, 34) in England worked with human hair, wool, quills and feathers, all of which were found to give essentially the same X-ray pattern. From the type of the pattern, which was similar to that of cellulose, they felt that, in general, they were dealing with small units of structure, rather than with units as large as those indicated by the high molecular weight of the protein, keratin, the principal constituent. Two types of X-ray patterns were found, Fig. 27 a and b, one from stretched



A



B

FIG. 27. DIFFRACTION PATTERNS FROM HAIR, TRANSFERRED TO BERNAL CHARTS; A, UNSTRETCHED; B, WHEN HAIR WAS STRETCHED TO DOUBLE ITS ORIGINAL LENGTH
(From Astbury)

hair, the other from hair in the normal unstretched condition. In both cases the patterns showed a definite repetition distance along the fiber axis; 5.15 Å for the normal condition and 3.4 Å for the stretched material. The pattern of the former gradually disappeared during the stretching process, and at the same time

the pattern of the stretched hair became more and more prominent until the extension had reached about 70 per cent of the original length, when the former had completely disappeared. Other changes in the X-ray patterns also occurred. Accompanying the change along the fiber axis, the two chief lateral spacings of 27 Å and 9.8 Å respectively of the normal hair gradually disappeared and narrower spacings, 4.65 Å and 9.8 Å replaced them in the stretched condition. These changes were interpreted as showing the unfolding of a long primary valence chain molecule making it thinner, and consequently drawing the chains closer together. The chain was considered as consisting of peptide linkage units as indicated above in connection with silk-fibroin, where the distance 3.5 Å between —CONH— units corresponded to 3.4 Å in the *stretched* hair; while the 5.15 Å distance of the normal hair corresponded to a folded condition as represented in Fig. 28. Wherever an R appears in the figure a residue of one of the several component amino acids is indicated. One of the 5.15 Å units represents three of the 3.4 Å peptide units when the hair is stretched. These interpretations were found to correspond quantitatively with the stretching measurements, and with other properties of hairs; and when taken altogether, they furnish a very reasonable picture of protein fibers. While it would be desirable to work with material which would give more clear cut X-ray diagrams, the present conception is acceptable until such material is forthcoming.

In addition to the proteinaceous materials already mentioned, other types have been examined by various investigators with the hope of finding one which would allow a more satisfactory X-ray analysis. Tendons, sinews and muscle tissues gave X-ray patterns but were far from satisfactory from the point of view of molecular structure; nevertheless they helped to build up a conception of the protein molecule. In a stretched condition, as opposed to a shrunken or contracted state, the change in pattern showed that there had been a rearrangement of particles of small molecular size, and when considered in connection with certain chemical and physical properties there seemed to be an indication here also of the existence of

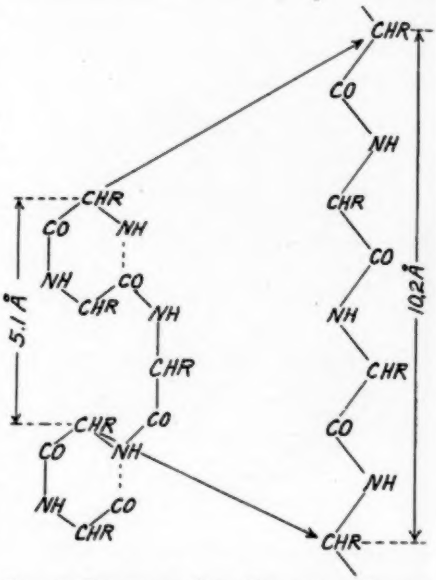


Fig. 28. Diagram to Show Relation of Folded Protein Molecule in Unstretched Hair (Left), to Stretched Molecule (Right)

long fibrous molecules (14). Further conclusions were for the most part speculative.

In summarizing the work done on structures which are built of protein materials, one feels no small degree of satisfaction in finding that the chemical units, amino acid residues, apparently remain intact as physical entities in the large protein molecule, or at least one may say that the evidence points very decidedly in that direction. Furthermore there seems to be

a definite interval which is repeated over and over in the length of the long protein molecule in spite of the fact that the units vary in size laterally, since each unit may be associated with a different kind of amino acid residue. The length of the interval fits well with the length of the three groups involved in a peptide linkage, thus allowing for the construction of a chain-like molecule of almost any length. The distance from chain to chain seems to be governed by the size of the

FIG. 29. X-RAY DIAGRAM FROM GELATIN (From Clark)

amino acid residues which project out from the sides of the chain.

These conclusions apply to structures of more or less permanent shape, which have considerable tensile strength. Structures of this kind not only seem to have long chain fiber-like molecules in their composition, but also to have these chain molecules placed in parallel arrangement forming the larger fiber-like structures. Proteins occur in the organism, also, in a more mobile form, where one would scarcely expect to find a parallel arrangement of the long molecules. An approach to the study of materials of this nature has been made through the use of gelatins and glues (32, 14). Comparatively little work has been done with them, and that, probably, out of curiosity as to whether they were amorphous or crystalline rather than as an attempt to determine their fine structure. Under certain conditions they were found to produce wide rings on the photographic plate when a pin-hole beam of X-rays was passed through them. The rings resembled somewhat those produced by liquids in general, except for the fact that they were more clear cut. In Fig. 29 a reproduction of such rings from gelatin is given. They indicate a certain degree of regularity in the arrangement of the molecules, suggesting the presence of minute pseudocrystalline particles in random arrangement.

MICELLES

In colloidal systems, whether sol or gel, as in most liquids, there is little question but that groups, minute aggregates, of molecules exist as individuals. To such aggregates Nägeli long ago gave the name "micelle." Their existence has been accepted as a fact not only in fluids, but, by most biologists, in organized bodies as well. Of course, much depends upon the definition of the word micelle, but when accepted as designating an entity, there may be a question as to whether such individuals exist as units in the more permanent structures which have been built up by vital processes. Proof of their existence in organized structures has been offered from many different fields of investigation including that of X-rays. It is only the latter in which we are interested here. Earlier in this paper in connection with X-ray reflection from cellulose fibers, it may be recalled that small blocks (Fig. 4) were assumed, for convenience of explanation, to exist as minute crystalline

components of the wall. Investigators have accepted their existence and, by measuring the width of the X-ray diffraction lines, have computed their dimensions (14). It must be remembered that in order to produce reflection, the molecular layers must be very uniform in spacing and in parallelism. A deviation of a very small part of a degree will cause the reflection from one plane to annul that from another in the same block. Thus if a minute piece of the cell wall, say as large as two of the small blocks mentioned, were bent very slightly in the middle, then one-half of it could be in a reflecting position while at the same time the other half would not, and, so far as X-ray reflection is concerned, the block would be only as large as the part which was in a reflecting position. A piece of material which was bent and warped in many places, only very slightly away from a uniform flatness, would give the effect of being made up of blocks set together unevenly. Any one who is accustomed to use the microscope much in biological work knows that a surface under high power may appear very irregular, which under low power was excessively smooth.

It seems then that the very minute warped and bent regions in organized structures might readily be mistaken for individual blocks, and measured by X-ray methods for micelles. Evidence from other sources leads one to believe that biological structures, even such as ramie fibers which show a considerable degree of uniformity in molecular arrangement, are not uniform throughout. In most cases they are layered structures with the interfaces between the layers lacking in orderly arrangement of the molecules. The layers, themselves, may be submicroscopic in thickness and are probably composed of still thinner layers. Their width and length are open to question, as also is the extent to which they may be connected tangentially, and perhaps radially, by anastomosing branches. Such a mesh-work structure seems to be not at all improbable, and if it does exist, the conception of the individuality of the micelle in such structures must be abandoned. When put into a colloidal liquid system the material of these mesh-work structures must be thought of as having been torn into minute particles which may then be considered as micelles. In many cases these micelles may have a regularity in the arrangement of their molecules, which approaches that of simple crystals.

FORCES INVOLVED

It may not be out of place, in concluding, to mention some of the concepts which emerge from studies of molecular structure such as have been reviewed briefly in this article. Obviously there are certain forces involved in holding atom to atom and molecule to molecule. An adequate discussion of these forces lies beyond the scope of this paper, but at least a word concerning them seems necessary. In a very general way it may be said, that primary valence forces hold the atoms together into a molecule, and further, that they are very strong forces; while on the other hand, the forces which hold molecules together are relatively much weaker. The latter may be spoken of collectively as van der Waals' forces. Primary valence forces are usually thought of as chemical forces, since in order to separate atom from atom a chemical reaction is necessary. In a cellulose chain the glucose residues are held together by primary valence forces acting through an oxygen bridge. In order to separate the residues from one another a chemical re-

action, hydrolysis, is necessary; but to separate the chains laterally, a simple swelling process is all that is needed to overcome the van der Waals' forces.

With these two conceptions in mind, one may visualize a possible process of cell wall growth (19). By diffusion, glucose molecules approach the surface of a cell wall. They are oriented into the proper positions necessary for units of the cellulose lattice and held here by van der Waals' forces. Their positions bring two OH groups of two adjacent glucose molecules close together, resulting, if conditions are suitable, in a chemical reaction in which one molecule of water is split off, and in the formation of the oxygen bridge between the glucose residues. A continuation of this process produces long chains of glucose residues having a strength due to the primary valence forces involved in the formation of the oxygen bridge. Such a structure should have great strength for small weight, for it is a very open structure, relatively, in terms of atomic structure.

At the surface of the wall one may conceive a layer one chain thick and many chains in width, literally a unimolecular sheet, with the chains held together laterally by van der Waals' forces. Since the glucose units of the chains are uniformly spaced they present a surface, with some sort of mosaic design, towards the protoplasmic matrix which forms an interface with it. The probability of a mosaic pattern being formed in the protoplasmic materials immediately adjacent is, to say the least of it, intriguing (33).

When one considers this surface layer in connection with a similar layer underneath it and visualizes more layers still deeper in the wall, as constituting the thickness of the cell wall, a molecular picture of a membrane begins to take form. But we are going beyond the limits set for this paper.

To one who is not conversant with this field of investigation, and who has managed to endure to this point, it is hoped that the spatial concept of the molecule may have a somewhat clearer meaning than heretofore; and that the concept may prove useful when thinking of activities which occur in the protoplasmic matrix of organisms, and of structures which are produced through so-called vital processes.

LIST OF LITERATURE

(1) Nägeli, C. 1858. Die Stärkekörner. Zurich.

(2) v. Laue, M., Friedrich, W., and Knipping, P. 1912. Sitzb. math-phys. Klasse bayer. Akad. Wiss., p. 303.

(3) Wyckoff, R. W. G. 1931. The Structure of Crystals. New York.

(4) Bragg, W. H., and Bragg, W. L. 1924. X-rays and Crystal Structure. London.

(5) Bragg, W. H. 1921. The structure of organic crystals. Proc. Phy. Soc. Lond., 34: p. 33.

(6) Sponsler, O. L. 1923. Structural units of starch determined by X-ray crystal structure method. Jour. Gen. Physiol., 5: pp. 757–776.

(7) Müller, A. 1923. The X-ray investigation of fatty acids. J. Chem. Soc. London, 123: p. 2043.

(8) Sponsler, O. L. 1925. X-ray diffraction patterns from plant fibers. J. Gen. Physiol., 9: 221–233.

(9) Wyckoff, R. W. G. 1922. Analytical expression of the results of the theory of space-groups. Carnegie Institution of Washington Pub. No. 318, Historical Introduction.

(10) Sponsler, O. L., and Dore W. H. 1926. The structure of ramie cellulose as derived from X-ray data. Colloid Symposium Monog. IV: pp. 174–202.

(11) Sponsler, O. L. 1926. Molecular structure of plant fibers determined by X-rays. Jour. Gen. Physiol., 9: pp. 677–695.

(12) Bragg, W. H., and Bragg, W. L. 1913. Structure of the diamond. Proc. Roy. Soc. (London), 89A: p. 277.

(13) Lewis, G. N. 1923. Valence and the structure of atoms and molecules. New York.

(14) Meyer, K. H., and Mark, H. 1930. Der Aufbau der hochpolymeren organischen Naturstoffe. Leipzig.

(15) Charlton, W., Haworth, W. N., and Peat, S. 1926. A revision of the structural formula of glucose. Jour. Chem. Soc., 129: pp. 89–101.

(16) Meyer, K. H., and Mark, H. 1928. Über den Bau des krystallisierten Anteils der Cellulose. Ber. d. d. chem. Gesell., 61: pp. 593–614.

(17) Sponsler, O. L. 1930. New data on cellulose space lattice. Nature (London), 125: pp. 633–634.

(18) ——. 1931. Orientation of cellulose space lattice in the cell wall. Protoplasma, 12: 241–254.

(19) ——. 1929. Mechanism of cell wall formation. Plant Physiol., 4: pp. 329–336.

(20) Freudenberg, K. 1931. Paper reported at Amer. Chem. Soc. meeting, Indianapolis.

(21) Hess, K., and Trogus, C. 1931. Zur Kenntnis der Faserperiode bei Cellulosederivaten. Zeit. f. physik. Chem., Bodenstein-Festband, pp. 385–391.

(22) Hendershot, O. P. 1924. Thermal expansion of wood. Science, 60: p. 456.

(23) Sponsler, O. L., and Dore, W. H. 1928. The structure of mercerized cellulose. Jour. Amer. Chem. Soc., 50: pp. 1940–1950.

(24) Nishikawa, S., and Ono, S. 1913. Transmission of X-rays through fibrous, lamellar, and granular substances. Proc. Math. Phys. Soc., Tokyo, 7: p. 131.

(25) Herzog, R. O., and Jancke, W. 1920. Röntgenspektrographische Beobachtungen an Zellulose. Zeit. Physik, 3: p. 196–197.

(26) Bernal, J. D. 1926. Interpretation of X-ray single crystal rotation photographs. Proc. Roy. Soc. (London), 113 A: p. 117.

(27) Müller, A. 1928. A further X-ray investigation of long chain compounds. Proc. Roy. Soc. (London), 120 A: p. 437.

(28) Bragg, W. H. 1930. Nature, 125: p. 634.

(29) Herzog, R. O., and Jancke, W. 1921. Festschrift der Kaiser Wilhelm-Gesellschaft.

(30) Brill, R. 1923. Über Seidenfibroin, I. Liebigs Annalen, 434: p. 204.

(31) Astbury, W. T., and Street, A. 1931. X-ray Studies of the Structure of Hair, Wool and Related Fibers. Phil. Trans. Roy. Soc. (London), 230A; pp. 75–101.

(32) Clark, G. L. 1927. Applied X-rays. New York.

(33) Sponsler, O. L. 1930. Discussion of surface structure in cell activity. Trans. Faraday Soc., 26: p. 813–814.

(34) Astbury, W. T., and Woods, H. J. 1932. Molecular structures of textile fibers. Jour. Textile Institute, 23: T17–T34.

(35) Sponsler, O. L. 1925. X-ray diffraction patterns from plant materials. Science, LXII: pp. 547–548.

THE EVOLUTION OF THE RESPIRATORY FUNCTION OF THE BLOOD

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(Contribution No. 13, Woods Hole Oceanographic Institution)

ACCORDING to current doctrines the mammals are the product of an evolutionary development which is traced back through the lower classes of vertebrates and is usually considered to have had its origin among the invertebrate phyla. In recent years the respiratory function of mammalian blood has been studied in great detail. Considered as a physico-chemical system concerned with the transport of oxygen and carbon dioxide, its characteristics are now well known and in many ways satisfactorily understood (35). Recent publications make it possible to compare these properties of the blood in at least one or more representatives of the various classes of lower vertebrates and of certain invertebrates. One can consequently inquire what changes in the characteristics of the blood parallel the supposed evolutionary development.

In considering the evolution of the vertebrates certain general tendencies are apparent which have an obvious relation to the respiratory function of the blood. In the first place, the change from an aquatic to a terrestrial habit of life involves a profound alteration in the method of aerating the blood and in the conditions to which the blood is exposed in the respiratory organs. In the second place, the general tendency throughout the development has led to organisms increasingly capable of intense activity. This has required the development of more effective arrangements for the circulation of the blood and the transport of gases by it in order to care for greater metabolic requirements. One of the factors which has favored the greater activity of which the birds and mammals are capable is the development of a constant, high body temperature which has at the same time fixed rather definitely one of the conditions under which the respiratory function of the blood takes place.

The transport of oxygen by vertebrate blood is due practically entirely to the hemoglobin present in it. Consequently the conditions under which oxygen is carried depend upon the specific properties of this substance. The transport of carbon dioxide, on the other hand, while depending in large part on reactions in which hemoglobin is involved, is a less specific phenomenon, since other proteins such as serum albumen and globulin and certain inorganic substances play a considerable rôle. The transport of carbon dioxide is consequently dependent in its details upon the general processes whereby the kidney and other organs regulate the composition of the blood.

The hemoglobins are substances which may be decomposed into hematin and a protein, globin. The former compound contains iron in complex combination with protoporphyrin. It is to the hematin fraction that the transport of oxygen by hemoglobin is due, oxygen being combined with hemoglobin in strict

proportion to its iron content. The hematins derived from the hemoglobin of different species appear to be identical, since it has been shown that the same porphyrin may be derived from the hematin of mammals, fish, and the insect, *Chironomus* (29) (48).

In addition to hemoglobin there are three other well-defined respiratory proteins. Chlorocruorin, which is most nearly related to hemoglobin, is found in the blood of certain worms,—the Sabellidae, Serpulidae, and Chlorhaemidae. Chlorocruorin is also a protein-hematin compound. The hematin, however, is not the same substance as that found in hemoglobin, being composed of a porphyrin distinct from that occurring universally in hemoglobin (32) (78) (79). Chlorocruorin has never been found in blood corpuscles, but occurs in solution in the blood and body fluids.

Hemerythrin is another respiratory protein containing iron which occurs in certain worms. This pigment does not appear to contain a hematin or a porphyrin and in certain other respects shares the characteristics of the hemocyanins (15) (53). Hemerythrin occurs in blood corpuscles, never in solution in the plasma. It is found in the blood of the Sipunculoidea, and in the polychaet, *Magelona*.

The hemocyanins, which are copper-protein compounds, show no chemical relation to hemoglobin and take no part in the respiratory function of the bloods which may be considered a part of the evolutionary series with which we are concerned.

The distribution of the hemoglobins in the animal kingdom is wide and, when considered from the point of view of evolutionary doctrine, puzzling. Hemoglobin is the universal respiratory pigment of the blood of vertebrates, being the only substance serving this function in the phylum and occurring in all its members with the exception of *Amphioxus*. It is also the dominant respiratory pigment in the annelid worms, occurring in the majority of polychaets and echiuroids, in many oligochaets and in some leeches (16) (50) (51) (64). In addition to these groups, where its distribution is somewhat general, hemoglobin is found in a variety of isolated instances in other parts of the animal kingdom, as the summary in Table 1 indicates.

In addition to its occurrence in the blood, hemoglobin is found in other tissues, particularly the muscles and nervous tissues of many animals. In the former situation it occurs in some forms which do not contain hemoglobin in their blood, for example, in the pharyngeal muscles of certain gastropods whose blood contains hemocyanin as the respiratory pigment (50) (54).

The occurrence of hemoglobin in these random cases among natural groups whose other members as a whole do not possess this substance is surprising from the evolutionary point of view. One can only conclude that it has been possible for hemoglobin to arise more or less independently in a variety of different groups. The difficulty is somewhat relieved by the discovery that protophorphyrin, the principal specific building-stone of hemoglobin, is widely distributed throughout the animal kingdom and by the demonstration that cytochrome, which like hemoglobin appears to be a porphyrin derivative, and allied pigments are very general in their distribution among plants and animals (1) (28) (30) (46). These considerations make it extremely dangerous to relate the vertebrate blood to that of any invertebrate group, for it appears quite possible that hemoglobin may have arisen *de novo* in the blood of the ancestral vertebrates just as it appears to have in

Chironomus, *Planorbis*, and other isolated instances. On the other hand, if the distribution of hemoglobin in the animal kingdom has any relation to evolutionary history, then emphasis must be placed on the fact that the annelids are the only invertebrate group in which the occurrence of hemoglobin is really general. In attempting to compare conditions existing in the blood of the vertebrates with those of lower animals, we are forced to assume this point of view, since the worms are the only group affording pertinent data with which we may deal.

TABLE 1

Distribution of Hemoglobin in the Blood of Animals

PHYLUM	CLASS	GENUS
Platyhelminthes	Turbellaria	*Derostoma* (56) *Syndesmis* (58)
	Nemertinea	*Drepanophorus* (39) *Polia* (50)
Nemathelminthes	Nematoda	*Ascaris* (46)
Molluscoidea	Phoronida	*Phoronis* (50) *Phoronopsis* (60)
Echinodermata	Holothuroidea	*Thyone* (16) *Cucumaria* (16) (71) *Caudina* (48a) *Malpadia* (48a)
Annulata	Polychaeta	Many cases (16) (64)
	Oligochaeta	Many cases (16) (64)
	Echiuroidea	*Thalassema* (51) *Urechis* (61)
	Hirudinea	Some cases (16)
Arthropoda	Crustacea	*Daphnia* (50) *Cheirocephalus* (50)
	Insecta	*Chironomus* (50)
Mollusca	Pelecypoda	*Solen* (50) *Arca* (16) (66) *Cardita* (85) *Pectunculus* (16)
	Gastropoda	*Planorbis* (50)
Chordata	All vertebrates	(50)

The conditions existing in the blood of the polychaet worms have been reviewed

amply by Romieu (64), who points out the great diversity of conditions occurring within this group. With a little freedom, his classification may be made to serve for the entire series in which hemoglobin occurs. Leaving out of account the large number of animals in which respiratory proteins do not occur, we find among the invertebrates two general situations which appear to include most cases. In those animals in which there exists a definite circulatory apparatus the respiratory pigment usually occurs in solution in the blood, which is sharply separated from a coelomic fluid, rich in leucocytes, and free from respiratory proteins. This is the most common situation among the polychaet worms and in the oligochaets. It is also the condition obtaining in those worms in which chlorocruorin occurs, except that in some at least of these forms chlorocruorin occurs also dissolved in the coelomic fluid, as in *Spirographis* and *Siphonostoma*.

In contrast there is a considerable number of animals in which the respiratory protein is enclosed in corpuscles and this situation occurs principally in those forms in which the vascular system is degenerate or lacking, the corpuscles being suspended in the coelomic fluid. This is the condition occurring in *Glycera*, *Capitella*, and *Polycirrus haematodes* among the polychaets, in the echiuroid *Urechis*, and in the sipunculoids *Phascolosoma* and *Sipunculus* in which the erythrocytes contain hemerythrin.

Two species of polychaets, *Terebella lapidaria*, and *Travisia Forbesii*, combine the two foregoing conditions. In these worms the vascular blood contains hemoglobin in solution, whereas the coelomic fluid is provided with abundant erythrocytes.

Finally, a single species of worm, *Magelona papillicornis*, exhibits a condition strictly comparable to that found in the vertebrates, that is, a blood confined to definite vessels in which the respiratory pigment is carried in blood corpuscles. The resemblance to the vertebrate condition is furthered by the fact that in *Magelona* alone, among all invertebrates, the blood corpuscles appear to be anucleated. The comparison to the vertebrate condition breaks down entirely, however, when it is considered that in *Magelona* the respiratory protein is hemerythrin.

The condition observed in *Phoronis*, *Phoronopsis*, and certain Nemertinea may best be classed with *Magelona*, for in these forms the blood is confined to definite vessels and contains erythrocytes bearing hemoglobin. The vascular system of the Phoronidae, however, is organized on somewhat different lines from those followed in the case of the worms and vertebrates.

From the foregoing it appears that although the situation under which hemoglobin occurs in the body fluids of the invertebrates is most varied, conditions which are strictly comparable to those found in the vertebrate series are rare and occur in rather isolated cases.

The general character of the erythrocytes found among the vertebrates is well known. It will suffice to recall that in all mammals, except in the camels, they are circular disc-shaped bodies. In the camels they are flattened ellipsoids. In the mammals they contain no nuclear material; in all other vertebrates they possess well-marked nuclei. In the birds, reptiles, amphibians and in all fishes except the cyclostomes, the erythrocytes are flattened ellipsoids; in the cyclostomes the shape is discoid (57).

The erythrocytes of the invertebrates are nucleated bodies, spherical in *Thalassema* (51) and *Urechis* (61), or flattened

discs of nearly circular outline, in *Terebella lapidaria*, *Glycera* (64), *Phascolosoma*, *Arca*, and *Thyone* (16a). The corpuscle is surrounded by a definite membrane which appears to enclose a distinctly fluid cytoplasm. In addition to the dissolved hemoglobin, the cytoplasm frequently contains highly refractive bodies, which Romieu considers to be fatty in nature, and also colored granules. These are thought to be accumulated waste materials by Romieu, who identifies them as a uratic pigment. Similar bodies are frequently very numerous in the erythrocyte of *Urechis*. Baumberger and Michaelis (8) consider the pigment to be hematin in this form and present evidence that the accumulation of hematin is utilized in forming the pigments of the egg. Romieu also presents a similar view with regard to the utilization of the pigments of the erythrocytes of *Terebella*. Rather extensive patterns of reticulation, resembling those of vertebrate erythrocytes, appear in the corpuscles of *Glycera*, *Phascolosoma*, *Arca*, and *Thyone* on treatment with brilliant cresyl blue (16a).

The invertebrate erythrocyte appears in general to be less highly differentiated than the vertebrate red blood corpuscle. Romieu's investigations indicate that the red cell found in the coelomic fluid of worms is strictly homologous to the vertebrate erythrocyte, the young corpuscle passing through all the phases which are known among the vertebrates. Jordan (40) believes that if one assumes a continuous evolution from invertebrates to vertebrates, a transition can be traced from segmented worms to cyclostome fishes in which the lymphogenous organ of invertebrates may be regarded as a very primitive spleen.

The apparent relation between the erythrocyte of the vertebrate blood and the corpuscle of the coelomic fluid in the invertebrates deserves some emphasis. Physiologists have tended to consider the occurrence of hemoglobin in solution in the blood of worms as representing a primitive condition and as such the evolutionary forerunner of blood containing erythrocytes. This view is definitely taken by Romieu (64), who suggests that the development of the coelomic erythrocyte has rendered the vascular system useless and has led to its degeneration in many forms. It has been maintained that the raison d'être of the erythrocyte is to permit hemoglobin to exist in the blood in quantities greater than would be possible were it dissolved directly in the circulating fluid (3). While it cannot be denied that the blood of the higher vertebrates contains more hemoglobin than could be dissolved in a fluid adapted to circulate in the vascular system, this possibility does not appear to have been realized in the invertebrate stage of evolution, for *Arenicola* and *Spirographis*, which carry their respiratory pigments in solution, have blood with a greater oxygen capacity than *Urechis* and the other invertebrate forms in which oxygen is transported in corpuscles (61). When these considerations are taken in connection with the fact that red blood corpuscles exist in such primitive forms as the nemerteans and *Phoronis*, one may properly question whether the occurrence of hemoglobin in solution in the blood of worms does not represent a rather specialized development. It seems significant in this connection that when hemoglobin occurs in solution it is always confined to a closed vascular system. It is now understood that the proteins of the plasma of the blood of the higher vertebrates play an important rôle in the hydrostatic equilibrium which determines the exchange of water through the capillary wall. It is known that fluids

free from protein or other substances of large molecular size cannot be retained within the vascular system. Is it not probable that the hemoglobin dissolved in the blood of the worms serves a function in counterbalancing the effect of the pressure developed within the blood vessels analogous to that exerted by the plasma proteins of the vertebrates? This action would not occur if the hemoglobin were retained in corpuscles unless other specialized serum proteins were developed to serve the purpose.

These considerations suggest that the hemoglobin which exists in solution in the blood of the invertebrates supplies a factor necessary in the hydrostatic equilibrium on which the existence of vascular blood depends. In the vertebrates the general occurrence of plasma proteins fulfills this requirement and makes it possible for hemoglobin to be confined to corpuscles suspended in the vascular fluid.

Certain quantitative facts appear to support this view. First, there is evidence of an increase in the concentration of plasma proteins in the evolutionary series. The body fluids of invertebrates are in general extremely poor in protein except for those cases where hemocyanin and the other respiratory proteins occur in solution. Among the worms, for example, there are no proteins in the coelomic fluid of *Echiurus pallasii* (68). In *Sipunculus* the concentration of protein in the coelomic fluid is 0.11 per cent (17); in *Urechis* 0.11 per cent (45). Among the vertebrates a progressive increase in the concentration of plasma protein occurs, the following values being recorded; skate, 2.4–3.1 per cent (20); dogfish, 2.2–4.4 per cent; goosefish, 1.4–2.2 per cent; menhaden, 0.72–2.9 per cent; bullhead, 3.9–4.8 per cent (52a); lungfish, 5.5 per cent (69); frog, 1.5–4.29 per cent (13); crocodile, 3.69 per cent (19); alligator, 4.4–5.8 per cent (2); snapping turtle, 4.8 per cent (35); dog, 6.1–6.7 per cent (21); man, 6.5 per cent (35). The increasing values appear to parallel the development of a cardiovascular system capable of containing blood at increasing pressures. In the second place, when hemoglobin occurs in solution in the blood, its concentration is comparable to that of the serum proteins in the lower vertebrates. It is estimated that the blood of *Planorbis* contains 1.5 per cent hemoglobin, that of *Arenicola* 3.25, that of *Lumbricus* 3.7 per cent (41). It is also pertinent that in the blood of *Syllidiens*, which contains no hemoglobin, the vascular blood contains a much larger quantity of protein than the perivisceral lymph (64). A more extensive investigation of the plasma proteins in the invertebrates and lower vertebrates is very desirable from this point of view.

THE QUANTITY OF HEMOGLOBIN IN THE BLOOD AND IN THE ERYTHROCYTE

Practical indication of the quantity of hemoglobin contained in the blood of various animals is given by measurements of the amount of oxygen with which it will combine when in equilibrium with atmospheric air. Representative data for various animals are presented in Table 2. In general there is an increase in the oxygen capacity of the blood in the course of the evolutionary series, the highest values of about twenty volumes per cent being found in the birds and mammals, the lowest values among the invertebrates. Within each group there is considerable variation which may be related directly to the activity of the various species. This is particularly well shown among the fishes (33). Table 2 also shows the way in which the volume of the blood occupied by cells tends to increase in the course of the evolutionary series. The ratio of

TABLE 2

The Oxygen Capacity and Cell Volume of the Blood of Various Animals

SPECIES	OXYGEN CAPACITY OF BLOOD	CELL VOLUME	OXYGEN CAPACITY OF 100 CC. CELLS
	vol. per cent	*per cent*	*vol. per cent*
Mollusks:			
Cardita sulcata (85)	1–2		
Pectunculus violaceus (85)	1–2		
Arca inflata (66)		6.5	
Planorbis corneus (10) (52)	1.0–2.5	None	
Insects:			
Chironomus (52)	6	None	
Worms:			
Urechis caupo (61)	2.7–7.2	18–40	9.3–17
Glycera siphonostoma (85)	2.6–3.0		
Arenicola marina (10)	8.4–9.7	None	
Spirographis Spallanzanii (32)	8.1–10*	None	
Fishes:			
Skate, *Raia ocellata* (20)	4.2–6.0	20	30
Dogfish, *Mustelus canis* (25)	5.5–7.8		
Goosefish, *Lophius piscatorius* (65)	5.1	15.5	33
Toadfish, *Opsanus tau* (65)	6.2	19.5	32
Puffer, *Spheroides maculatus* (65)	6.8	17.5	39
Scup, *Stenotomus chrysops* (65)	7.3	32.6	23
Sea robin, *Prionotus carolinus* (65)	7.7	24	32
Carp, *Cyprinus carpio* (23) (80)	11.5–16.8	40	35
Mackerel, *Scomber scombrus* (65)	15.8	37	43
Eel, *Anguilla japonica* (43)	10.2–15.6	31–41	35
Amphibians:			
Amphiuma tridactyla (67)	2.5–8.4	14–28	25
Rana esculenta (23) (84)	13.5–23	41	33
Reptiles:			
Snapping turtle, *Chelydra serpentina* (35)	5.9	20.4	29
Tortoise, *Pseudemys concinna* (70)	6.6–11	9.8–22	50
Alligator (38)	12	14.5	83
Crocodile, *Crocodilus acutus* (19)	8–10	18–24	43
Birds:			
Sparrow (23)	14.5	37	39
Serin (23)	14	36	39
Pigeon (23)	21	53	40
Surf scooter (60)	22	45	47
Crow (23) (83)	17–22	54	40
Owl, *Syrnium aluco* (83)	19		
Mammals:			
Man (24)	21	46	46
Horse (24)	16.7	36	47
Sheep (24)	15.8	39	41
Rat (24)	18.7	47	40
Sea lion, *Eumetopias stelleri* (31)	19.8	29	68
Porpoise (70a)	42–45		
Porpoise, *Phocaena phocaena* (32b)	22.2	35	63

* Blood contains chlorocruorin.

oxygen capacity to the volume of cells in a unit quantity of blood, tabulated in the fourth column, shows how the concentration of hemoglobin varies in the red corpuscles of the different groups. These data exhibit a very definite trend. The concentration of hemoglobin in the erythrocyte of *Urechis* is much less than that observed in any vertebrate. The values are relatively constant among the fish and amphibians and are highest in certain reptiles, birds, and mammals. The highest values are found in the aquatic mammals. (The exceptionally high value obtained for the alligator would appear to require confirmation in view of its dissimilarity from that characterizing the crocodile and other cold-blooded vertebrates.) The progressive morphological differentiation which the erythrocytes show throughout the animal series is accompanied by a definite increase in the concentration of hemoglobin within them.

THE EQUILIBRIUM BETWEEN HEMOGLOBIN AND OXYGEN

The equilibrium between oxygen and the hemoglobin of the blood is commonly expressed by the so-called "oxygen dissociation curve" in which the amount of oxygen combined with the blood, expressed as a fraction of the total oxygen capacity, is plotted against the partial pressure of oxygen with which the blood is in equilibrium (Figs. 1 and 2). Although more than half a dozen theories have been proposed, the interpretation of the exact shape of such curves is not altogether clear (5) (27). For purposes of description the oxygen dissociation

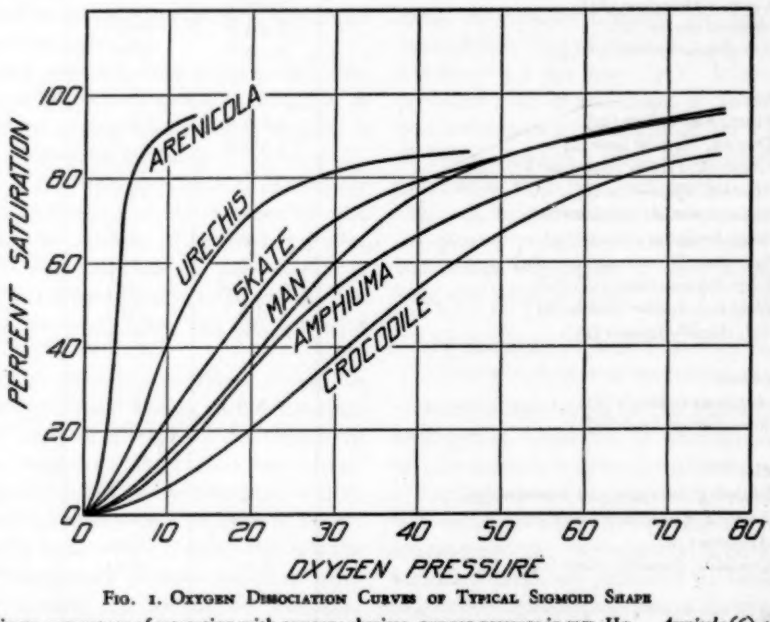

FIG. 1. OXYGEN DISSOCIATION CURVES OF TYPICAL SIGMOID SHAPE

Ordinate, percentage of saturation with oxygen; abscissa, oxygen pressure in mm. Hg. *Arenicola* (6), 20°C., pH 6.9; *Urechis* (61), 19°C., pH 7.1; skate (20), 10.4°C., pH 7.8; man (35), 38°C., pH 7.47; *Amphiuma* (67), 26°C., carbon dioxide pressure 43 mm.; crocodile (19), 29°C., pH 7.2.

curves of most bloods are defined with sufficient precision by Hill's (37) equation

$$y = 100 \frac{Kx^n}{1 + Kx^n}$$

in which y is the percentage of the hemoglobin oxygenated at the partial pressure of oxygen, x. The general shape of the oxygen dissociation curve is related to the value of n. For a hyperbolic curve, n is 1.0; at higher values of n (above about 1.4) the curve acquires a double inflexion or S-shape which becomes more marked as the value of n increases.

The shape of the oxygen dissociation curve, as indicated by n, appears to be affected little or not at all by temperature (11) (81) and by changes in hydrogen ion concentration or carbon dioxide pressure (5) (27). This fact simplifies the comparison of the shape of the oxygen dissociation curves of different species, since the differences in the conditions under which the measurements have been carried out may be neglected. The value of n characteristic of different bloods varies considerably as the following table shows:

	n
Skate (20)	2.0
Eel (44)	1.0
Carp (80)	1.3
Amphiuma (67)	1.8
Turtle (70)	1.5
Man (5)	2.2
Pig (11)	2.0–2.6
Ox (11)	2.3–3.0

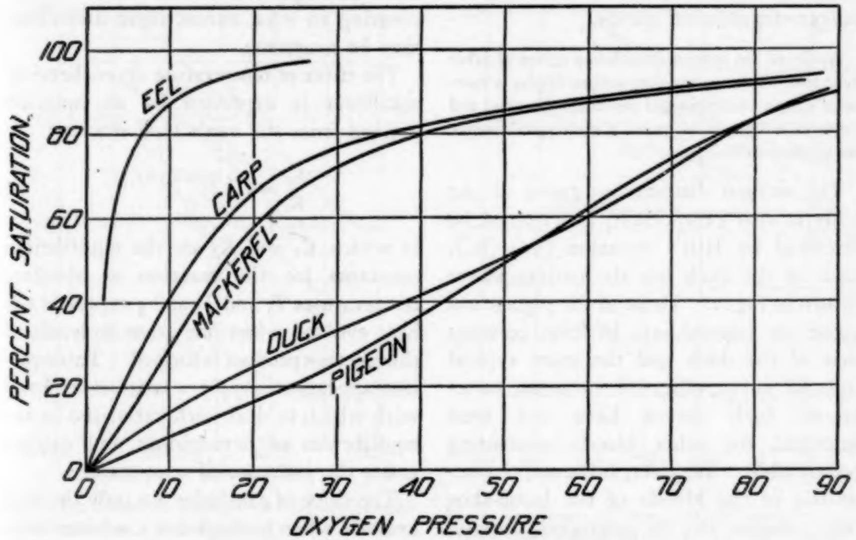

Fig. 2. Oxygen Dissociation Curves of Atypical Shape

Ordinate, percentage of saturation with oxygen; abscissa, oxygen pressure in mm. Hg. Eel (44), 17°C., carbon dioxide pressure not given; carp (80), 18°C., carbon dioxide pressure 30 mm.; mackerel (65), 20°C., carbon dioxide pressure 1 mm. Hg.; duck (81), 42°C., carbon dioxide pressure 40 mm.; pigeon (81), 42°C., carbon dioxide pressure 40 mm.

The bloods of the great majority of animals show a distinctly S-shaped oxygen dissociation curve, as indicated by the higher values of n. This is true of the mammals, the crocodile (19), *Amphiuma*, the skate, and the worms *Urechis* (61)

and *Arenicola* (6). The oxygen dissociation curves of the blood of fish appear to be somewhat exceptional in that the sigmoid character of the curve is less pronounced (in the mackerel) or is lacking as in the sea robin, toadfish (65), and carp (80). The blood of the eel is said to have a purely hyperbolic oxygen dissociation curve, but the evidence for this cannot be considered convincing. Figure 2 illustrates the form of some of these atypical oxygen dissociation curves.

Studies of the oxygen dissociation curves of fishes made since the foregoing was written display a number of unique conditions not previously described and throw some light on the nature of the atypical oxygen dissociation curves (32c).

The oxygen dissociation curve of the birds is also exceptional, and cannot be described by Hill's equation (81) (82). That of the duck has the curious shape shown in Fig. 2. Those of the pigeon and goose are intermediate in form between that of the duck and the more typical sigmoid curve observed in most vertebrates. Such curves have not been described for other bloods containing hemoglobin. They are, however, characteristic of the bloods of the horse-shoe crab, *Limulus*, and the gastropod, *Busycon*, which contain hemocyanin (60).

The comparative study of the equilibrium of blood with oxygen is complicated by the variety of factors which influence the degree of oxygenation which will be attained under any given oxygen pressure. This relation is defined by the value of the oxygen dissociation constant K in Hill's equation. Certain of these factors are inherent in the chemical properties of the medium in which hemoglobin exists in the blood. Others, such as temperature, are determined purely by the environmental conditions in most forms, while some factors, such as carbon dioxide tension and hydrogen ion concentration, are influenced alike by physiological and environmental considerations. It is frequently difficult to compare the data obtained by various observers because each has been concerned with a somewhat different aspect of the problem and it is infrequent that data are obtained under strictly comparable conditions. It is consequently desirable to consider some of the factors affecting the equilibrium of oxygen with hemoglobin with a view to discovering to what extent these difficulties may be overcome.

The effect of temperature upon chemical equilibria is expressed by an equation derived from the van't Hoff isochor:

$$\frac{K_2}{K_1} = e^{-q(T_2 - T_1)/RT_1T_2}$$

in which K_1 and K_2 are the equilibrium constants for the reaction at absolute temperatures T_1 and T_2 and q expresses the heat evolved when one gram molecule of the reaction product is formed. This equation appears to supply a satisfactory basis with which to deal with variations in the equilibrium of hemoglobin and oxygen under the influence of temperature.

The value of q includes not only the heat evolved when hemoglobin combines with oxygen, but, as commonly measured, the heat of solution of oxygen and such other heat exchanges as accompany the altered equilibria which occur when blood is oxygenated. The latter are due chiefly to the fact that hemoglobin becomes a stronger acid when oxygenated and in consequence a new equilibrium is established in the distribution of base between hemoglobin, bicarbonate and perhaps other weak acids. Since it has been shown that in the case of the blood of the pig, ox (11), pigeon, duck, and goose (81) (82) the shape of the oxygen dissociation curve is unchanged by variations in temperature, in practice the reciprocal of p_{50},

the oxygen tension at which the blood is half saturated with oxygen, may be substituted for the equilibrium constant. The data may be expressed by plotting the logarithm of p_{50} against the reciprocal of the absolute temperature when it is found that the experimental points fall on a line which is straight, or nearly so, and with a slope which is determined by q. When

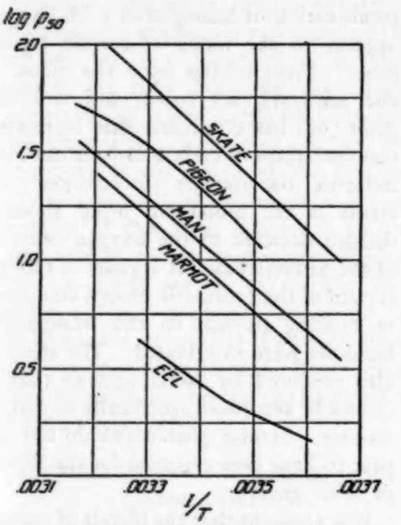

FIG. 3. THE EFFECT OF TEMPERATURE ON THE TENSION OF OXYGEN AT WHICH THE BLOOD IS HALF SATURATED WITH OXYGEN

Ordinate, log p_{50}, the logarithm of the tension of half saturation. Abscissa, $1/T$, the reciprocal of the absolute temperature. Skate (20), CO_2 tension 1 ± 0.5 mm.; pigeon (81), CO_2 tension 40 mm.; man (11), CO_2 tension 40 mm.; marmot (26), CO_2 tension 40 mm.; eel (44), CO_2 tension not given.

blood is studied under suitable conditions, q has very nearly the same value in a considerable number of species. This is brought out by the fact that the various curves illustrated in Fig. 3 have about the same slope. Such similarity is only to be expected if the heat of reaction between hemoglobin and oxygen is about the same in all species and provided the conditions are such that the accessory reactions accompanying oxygenation absorb an equal fraction of the heat of reaction in each case. These facts point to a general similarity in the blood of different forms in respect to the thermodynamic changes involved in the combination of hemoglobin with oxygen. When the experiments are carried out at diminishing carbon dioxide pressures (7) (81), in the

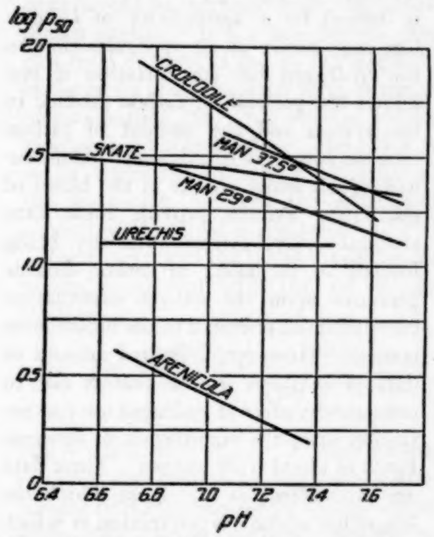

FIG. 4. THE EFFECT OF HYDROGEN ION CONCENTRATION UPON THE PRESSURE OF OXYGEN AT WHICH BLOOD IS HALF SATURATED WITH OXYGEN

Ordinate, log p_{50}, the logarithm of the tension of half saturation; abscissa, hydrogen ion concentration expressed in pH units. Crocodile (19), 29°C.; man (35), 37.5°C. and (19) 29°C.; skate (20), 10.4°C.; *Urechis* (61), 19°C.; *Arenicola* (6), 20°C.

absence of carbon dioxide (11), or at constant hydrogen ion concentration (26), temperature changes have a larger effect upon the value of the equilibrium constant, and the heat of reaction is larger when measured directly, than is the case in experiments done under constant carbon dioxide pressures of normal physiological value. This is explained by the diminished degree to which heat is absorbed

through changes in the quantity of base combined with the hemoglobin.

The effect of hydrogen ion concentration upon the equilibrium of various bloods with oxygen is more difficult to deal with. The hydrogen ion concentration, depending as it does on the ratio of acids and bases in the blood and upon the equilibria which determine the distribution of electrolytes between corpuscles and plasma, is defined by a multiplicity of factors. One may arrive at an approximation to the hydrogen ion concentration if one knows the pressure of carbon dioxide in the system and the amount of carbon dioxide bound as bicarbonate. Unfortunately, not many studies of the blood of the lower animals provide these data simultaneously, attention usually being limited to the effect of carbon dioxide pressures upon the oxygen dissociation curve without reference to the bicarbonate content. However, a limited amount of data is available which enables one to compare the effect of hydrogen ion concentration upon the equilibrium of different kinds of blood with oxygen. These data are summarized in Fig. 4, in which the logarithm of the oxygen tension at which the hemoglobin is half saturated with oxygen is plotted against the pH of the blood. The facts summarized in this figure make it clear that the various bloods vary distinctly in regard to the effect of hydrogen ion concentration upon the equilibrium of blood with oxygen. In some bloods, as that of the skate at acid reactions, and that of *Urechis*, the hydrogen ion concentration has little or no effect on the oxygen equilibrium. In most of the bloods which have been studied the effect is marked, its magnitude differing from species to species. If the data presented in Fig. 4 are corrected to some uniform temperature employing the principle set forth above, the agreement among the various species is not improved. It seems probable that these variations are due to specific differences in the hemoglobin of the different animals. From the available data it is impossible to see any definite tendencies which may be related to the systematic classification of the animals.

A somewhat special relationship between hydrogen ion concentration and the combination of hemoglobin with oxygen appears in the blood of certain teleost fishes. From studies upon the blood of the mackerel, sea robin, and toadfish, Root (65) has concluded that increasing concentrations of carbon dioxide not only influence the oxygen dissociation constants of the blood but bring about a decided decrease in the oxygen capacity of the hemoglobin. It appears as though certain of the prosthetic groups concerned in binding oxygen to the hemoglobin molecule were inactivated. The effect is also produced by lactic acid so that it cannot be attributed specifically to carbon dioxide. Similar phenomena do not appear to have been recorded for the bloods of other groups.

It is apparent that the bloods of various animals differ markedly in the conditions governing the equilibrium with oxygen. This fact may be most simply explained on the assumption that the hemoglobins of the different species are chemically distinct. For this view there is some evidence of a spectroscopic, crystallographic and chemical sort (5) (34) (48a) while immunological experiments indicate that the carbon monoxide hemoglobin from different mammals is species specific (9).

The nature of the chemical differences in different hemoglobins is, however, still quite illusory. Since the porphyrin portion of all hemoglobins appears to be the same (29) (48), it has generally been

suspected that the specific qualities of hemoglobin depend upon the globin fraction of the molecule. Investigations of globin as yet do not appear to have demonstrated the nature of such specific differences if they exist (63).

It has also been suggested that the specific differences may be due to the occurrence of hemoglobin within semi-permeable corpuscles which enables a characteristic chemical environment to be secured for the hemoglobin of each species and thus determines its specific properties in each organism. Against this view it may be pointed out that the properties of the blood of the dog are very similar to those of the blood of man in spite of the great differences in the composition of the corpuscular electrolytes in these species (21). The two views are not mutually exclusive. In the absence of any studies of the properties of the purified proteins of the lower forms it is impossible to evaluate the importance of either possibility.

THE EQUILIBRIUM OF THE BLOOD WITH CARBON DIOXIDE

Carbon dioxide is transported in the blood as bicarbonate which results from the union of this gas—as carbonic acid—with base derived from hemoglobin, serum proteins and other buffers. It is not surprising consequently that the carbon dioxide dissociation curves of most animals are similar in form, and differ chiefly in the quantity of bicarbonate formed under a given carbon dioxide pressure. The curves shown in Fig. 5 illustrate this. It should be noted that the height of the curves from the base line follows in general the order of increasing hemoglobin content—as indicated by the recorded oxygen capacities of the blood.

The blood of a certain group of animals exhibits carbon dioxide dissociation curves which differ distinctly from the typical form. These are the bloods of the turtle (70), frog (84), *Amphiuma* (67), and carp (80). The carbon dioxide dissociation curves of these forms illustrated in Fig. 6. are all very much higher and flatter than those of the bloods exhibiting the more usual condition and indicate a greater ability to combine with carbon dioxide than would be expected from the hemoglobin content. It has been shown that this form of curve is due to the retention in the blood of an unusually large quantity of bicarbonate (67) (70) relative to the hemoglobin concentration. The effect is to be attributed to some peculiarity in the mechanism whereby the electrolyte content of the blood is regulated.

The buffering of the blood may be more precisely analyzed with the aid of the relation

$$\beta = \frac{-\Delta\ BHCO_3}{\Delta\ pH} = \frac{-\Delta\ BHCO_3}{\Delta \log \frac{BHCO_3}{H_2CO_3}}$$

where the buffer value, β, is given by the ratio of the change in the bicarbonate content to the accompanying change in pH when the carbon dioxide pressure is increased (72). In the invertebrates it appears that the respiratory protein itself is the principal, if not the sole buffer substance. In *Limulus* the hemocyanin accounts for practically the total buffer effect (62). In *Urechis* the coelomic fluid appears to contain practically no buffers. The total buffer action is exerted by virtue of the corpuscles and their buffer value is equal to that of a quantity of human hemoglobin having an equivalent oxygen content (61). In the vertebrates also the buffer value of the blood as a whole when compared on the basis of equivalent oxygen capacity is approximately the same in the case of the skate (20), turtle (70), crocodile (19), dog (20), and man

(19). This general relation is reasonable, from the physiological standpoint, for under ordinary circumstances the carbon dioxide production of animals is nearly equal to oxygen consumption so that the needs for transport of the two gases go hand in hand. Table 3 summarizes the buffer value of the hemoglobin in the corpuscles of a number of different animals.

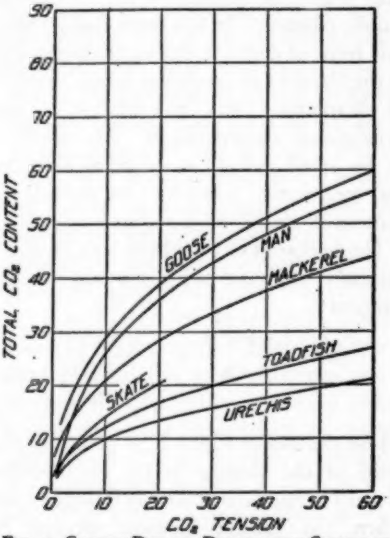

FIG. 5. CARBON DIOXIDE DISSOCIATION CURVES OF TYPICAL SHAPE

Ordinate, total carbon dioxide content measured in volumes per cent; abscissa, partial pressure of carbon dioxide measured in mm. Hg.

	Temperature °C	Oxygen capacity vol. per cent
Goose (83)	40	20
Man (35)	38	20
Mackerel (65)	20	15.8
Skate (20)	25	4.2–6.0
Toadfish (65)	20	6.2
Urechis (61)	18.5	3.9

The blood of vertebrates contains serum proteins which contribute definitely to the buffer value of the blood. It has been pointed out that the serum proteins are present in increasing concentration in the blood of the higher members of the vertebrate series. The relative part played by the serum proteins in buffering the blood against carbon dioxide is indicated in Table 4. The last column in this table indicates the relation of the buffer value of the serum proteins to their concentration in the blood and shows that the serum proteins in the skate and crocodile are more effective buffers than those in man. In this way they compensate in

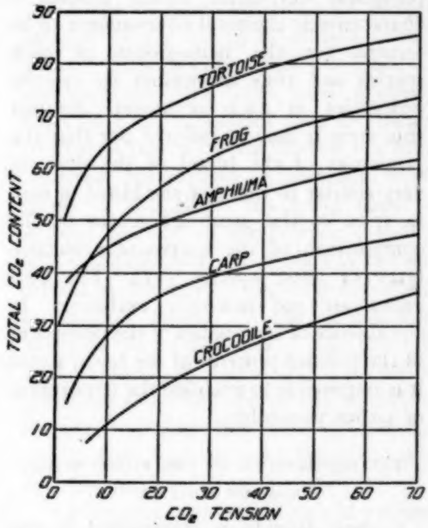

FIG. 6. CARBON DIOXIDE DISSOCIATION CURVES OF ATYPICAL SHAPE

Ordinate, total carbon dioxide content measured in volumes per cent; abscissa, partial pressure of carbon dioxide measured in mm. Hg.

	Temperature °C	Oxygen capacity vol. per cent
Tortoise (70)	25	ca. 9
Frog (84)	15	ca. 10
Amphiuma (67)	24	ca. 5
Carp (80)	15	ca. 9
Crocodile (19)	29	9.25

part for their lower concentration. Serum proteins are inferior buffers compared to hemoglobin as the recorded buffer values show.

In the Mammalia a large portion of the transport of carbon dioxide from the tissues to the lungs is effected as the result

TABLE 3

Buffer Values of Hemoglobin in Corpuscles at Physiological Reactions

SPECIES	BUFFER VALUE
	milliequivalents per gram hemoglobin
Urechis caupo, 19° (61)	0.169
Crocodilus acutus, 29° (19)	
Oxygenated	0.208
Reduced	0.143
Man, 29° (19)	
Oxygenated	0.183
Reduced	0.159
Man, 37.5° (18)	
Oxygenated	0.186
Reduced	0.166
Horse, 38° (74)	
Oxygenated	0.158
Reduced	0.147

In computing these values it is assumed that the equivalent weight of hemoglobin is 16,700 in all three species. The buffer value of the hemoglobin of the horse is based on studies of crystalline hemoglobin. That of other species is deduced from the study of whole blood.

TABLE 4

Buffer Values of Whole Blood, Separated Serum and Serum Proteins

SPECIES	TOTAL BLOOD OXYGENATED	TOTAL SERUM SEPARATED	SERUM PROTEINS
	milliequivalents per liter	*milliequivalents per liter*	*milliequivalents per gram protein*
Urechis caupo, 19° (61)	4.9	0	0
Skate, *Raia ocellata*, 25° (20)		4.63–6.48	0.193–0.209
Crocodile, *Crocodilus acutus*, 29° (19)	18.2	4.87	0.132
Dog, 37.5° (21)			0.093
Horse, 38° (75) (76) (77)	25.26		0.068–0.104
Man, 37.5° (36)	26.2	7.5	0.109

The buffer values for serum proteins of the horse are based on dialyzed serum (0.068) and purified serum proteins (0.104). The values for other animals are deduced from studies of plasma without correction for small amounts of other buffer substances.

of the fact that oxyhemoglobin is a stronger acid than reduced hemoglobin. At any carbon dioxide tension, reduced blood will combine somewhat more of this gas than will oxygenated blood. A similar effect has been observed in a large number of vertebrate bloods, although in some species it is necessary to concentrate the corpuscles before the effect is large enough to be clearly measurable. The effect is absent, or at least undetectable, in the blood of *Urechis* and of the skate. In these forms the reciprocal phenomenon, in which the presence of carbon dioxide affects the equilibrium between hemoglobin and oxygen, is absent (in *Urechis*) or very slightly developed (in the skate). Table 5 shows the magnitude of the change in bicarbonate content with change in oxygen content of the blood of a variety of animals. It is clear that this property of the blood varies definitely in different animals. Since the relation is a function of the properties of hemoglobin, it is probable that the differences observed in the various species are due to specific differences in their hemoglobins.

Although hemoglobin is the principal buffer substance concerned with the transport of carbon dioxide in the blood, this gas, unlike oxygen, is not confined to the corpuscles, but is distributed according to well-recognized principles between the corpuscles and plasma (73). The hemo-

globin within the corpuscle is able to contribute to the buffer value of the plasma by reacting with anions, chiefly chloride, which migrate into the corpuscles from the plasma. The excess of cations thus set free in the plasma can consequently combine with carbonic acid to form bicarbonates. A similar phenomenon appears to occur in the blood of *Urechis* (61), the turtle (70), the crocodile (19), and the hen (14) and is doubtless a general phenomenon. In these forms the facts have not been studied in detail, and

TABLE 5

Effect of Oxygenation upon the Carbon Dioxide Content of Bloods at Constant Hydrogen Ion Concentration

The values are for a pH of 7.2 to 7.4 or when log $\frac{BHCO_3}{H_2CO_3} = 1.0$.

SPECIES	$\frac{-\Delta BHCO_3}{\Delta O_2}$
Urechis caupo (61)	0
Skate, *Raia ocellata* (20)	0
Toadfish, *Opsanus tau* (65)	0.45
Sea robin, *Prionotus carolinus* (65)	0.45
Mackerel, *Scomber scombrus* (65)	0.70
Amphiuma tridactyla (67)	0.54
Tortoise, *Pseudemys concinna* (70)	0.32
Snapping turtle, *Chelydra serpentina* (35)	0.22
Crocodile, *Crocodilus acutus* (19)	1.05
Caiman fuscus (19)	0.56
Goose (82)	0.50
Horse (75)	0.55
Man (35)	0.49

the quantitative aspects of the factors governing the distribution of anions and cations between corpuscles and plasma are not altogether clear. Since these animals all possess a relatively small volume of corpuscles, the phenomenon is of particular importance in that it allows most of the carbon dioxide to remain in the plasma where it is distributed through a volume large in comparison to that of the corpuscles which retain the hemoglobin.

RÉSUMÉ

The properties of the blood of the vertebrates and their forerunners display great variety in their quantitative relationships. In reviewing them, certain general tendencies have appeared. The variety of situations in which hemoglobin occurs in the invertebrates disappears in the vertebrates, among which the hemoglobin is universally confined within corpuscles in the blood. The morphological differentiation of the erythrocyte, which continues through the vertebrate series, is accompanied by an increased concentration of hemoglobin within the corpuscle. This tendency, coupled with an increase in the quantity of corpuscles in the blood, has led to a greater oxygen-carrying capacity in the more highly developed members of the series, and in the more active representatives of the lower groups. In turn the carbon dioxide-combining capacity and buffering powers of the bloods have increased with increasing hemoglobin content.

Throughout the series there has been a tendency for the plasma proteins to increase. This development is probably related to the hydrostatic conditions within the blood vessels and parallels an increase in the blood pressure in the various groups, but it contributes somewhat to the buffer power of the blood. A special tendency of the blood to contain a large quantity of bicarbonate appears in certain of the lower freshwater vertebrates, giving them a specialized type of carbon dioxide dissociation curve.

Throughout the series the respiratory properties of the blood are dependent upon hemoglobin, and the general properties of this substance are displayed in general by all forms. Thus the effect of temperature on the oxygen equilibrium and the buffer action of hemoglobin appear to be very similar throughout. All

hemoglobins, with the exception of that of *Urechis* and under some circumstances the skate, exhibit the remarkable reciprocal relation between oxygen, carbon dioxide, and the products of their reaction with hemoglobin.

Quantitatively, however, there is clear individuality in the behavior of the hemoglobin of the different species. This appears in the shape of the oxygen dissociation curve, particularly in birds and fishes; in the oxygen pressures necessary to cause the hemoglobin to unite with oxygen; in the magnitude of the effect of altered hydrogen ion concentration on these pressures; and reciprocally in the effect of oxygenation and reduction on the quantity of carbon dioxide with which the blood will combine.

To what extent may these developments, quantitative or qualitative, be related to the special physiological problems faced by the respiratory mechanism of the various animals?

PHYSIOLOGICAL CONSIDERATIONS

Early students of the distribution of hemoglobin among the invertebrates were struck with its sporadic occurrence and pointed out that the possessors of this substance were animals which lived in places in which the oxygen supply is limited. It was suggested that hemoglobin developed in response to this situation, and that the substance provided a useful reservoir of oxygen for use in times of need. This suggestion was examined by Miss Leitch (52), who showed that in *Planorbis* the supply of oxygen combined with hemoglobin was only sufficient to last the animal for three minutes and consequently could not be considered seriously as a provision for prolonged anaërobic existence. The oxygen storage theory has been reviewed by Barcroft (6), who pointed out that the oxygen combined with *Arenicola* blood is sufficient to meet the requirements of the worm for an hour or thereabouts and will thus serve to tide over the period when the animal closes its burrow at low water. A somewhat similar situation occurs in *Sipunculus* (12) and *Urechis* (61). In the latter the oxygen content of the blood is sufficient to last about an hour, and probably serves during the prolonged periods of rest when respiratory activity is interrupted.

Borden (10) has re-examined the matter in a careful study of *Planorbis corneus* and *Arenicola marina*. She finds that the blood of *Planorbis* can combine enough oxygen to last 18 minutes and that this together with the air entrapped in the lung is sufficient to enable the snail to endure an hour's subjection to oxygen deficiency. She concluded that in both *Planorbis* and *Arenicola* the function of the hemoglobin is to carry oxygen when the animals are subjected to low oxygen pressures, but that the importance of hemoglobin as a temporary store is not negligible in either species. There can be no doubt that the oxygen capacity of the blood is important in enabling animals to resist short periods of suspended respiration, as in whales and diving birds, but it is significant that high oxygen capacities are developed in those forms which are most dependent on an abundant oxygen supply, as in the pelagic fish, birds, and mammals, and not in those which dwell in poorly aërated regions. Animals which are resistant to oxygen-lack frequently are devoid of respiratory pigment and their resistance appears to depend rather on other qualities of their tissues.

The proper significance of hemoglobin in relation to the oxygen of the environment was clearly shown by the experiments of Miss Leitch on *Planorbis* and

Chironomus. She found that in these forms the hemoglobin is fully oxygenated when the animals are in well-aërated water. Under such circumstances the solubility of oxygen in the body fluids is sufficient to meet all metabolic requirements. It is not until the oxygen pressure in the water has fallen to 50 mm. in *Planorbis*, and 7 mm. in *Chironomus*, that the oxygen combined with the hemoglobin is utilized. These forms are able to live in water poor in oxygen because their hemoglobin will take up oxygen at low pressures and transport it to the tissues. The condition appears to be similar in the earthworm (22) (42) and *Urechis* (61).

Krogh and Leitch (49) have extended this view to explain the pressures at which the blood of fishes combines with oxygen. Using the tension of oxygen at which the blood is half saturated as an index, they pointed out that in fresh-water fishes, such as the carp, eel, and pike, which are occasionally exposed to low oxygen pressures, the tension of half

TABLE 6

Tension of Oxygen at Which Various Bloods Are Half Saturated under Approximately Physiological Conditions

SPECIES	TEMPERATURE	pH	CARBON DIOXIDE PRESSURE	OXYGEN TENSION OF HALF SATURATION
	°C.		mm. Hg	mm. Hg
Planorbis corneus (87)	20		0?	6.0
Arenicola (6)	20	7.3	7.3	1.8
Urechis caupo (61)	19	7.1	7.1	12.0
Siphunculus nudus (30a)	19		0–80	8.0*
Spirographis Spallanzanii (32a)	20	8.0		14.0†
Skate, *Raia ocellata* (20)	10	7.8	1.0	20.0
Mackerel, *Scomber scombrus* (65)	20		1.0	17.0
Sea robin, *Prionotus carolinus* (65)	20		1.0	16.0
Toadfish, *Opsanus tau* (65)	20		1.0	14.0
Cod (49)	15		0?	18.0
Plaice (49)	15		0?	10.0
Trout (49)	17		0?	11.0
Carp (80)	18		30	9.6
Carp (49)	17		0?	2–3
Pike (49)	17		0?	2–3
Eel (49)	17		0?	2–3
Amphiuma tridactyla (67)	26		43	28
Rana esculenta (87)	20		0?	10
Tortoise, *Pseudemys concinna* (70)	25		40	20–30
Snapping turtle, *Chelydra serpentina* (35)	20		42	22
Crocodile, *Crocodilus acutus* (19)	29	7.2		38
Pigeon (81)	42		40	50
Duck (81)	42		40	50
Goose (82)	42		50	37.5
Horse (35)	38	7.46	41	26
Man (35)	38	7.47	41	26
Sea lion, *Eumetopias stelleri* (31)	38		44	40
Porpoise, *Phocaena phocaena* (60)	38	7.25	46	31

* Blood contains hemerythrin.

† Blood contains chlorocruorin.

saturation is comparatively low as compared to marine fish, the cod and plaice, and such fresh-water fish as the trout, which are not normally exposed to very low oxygen tensions. They considered the properties of the blood in both cases to be specially adapted to the biological conditions.

In order that the data which have since accumulated may be considered from this standpoint Table 6 has been prepared. In it are entered the tensions of oxygen at which the bloods of the various species are half saturated under conditions of hydrogen ion concentration, carbon dioxide pressure, and temperature as near to those obtaining in the circulation of the living animal as can be, in view of the available data. The full oxygen dissociation curves for some of the bloods under these conditions are shown in Figs. 1 and 2. So far as the fishes are concerned, the newer data on the marine forms, the skate, mackerel, toadfish, and sea robin, fall within the limits set by the marine forms studied by Krogh and Leitch. *Arenicola* comes up to expectation in having a very low working tension. It is difficult to see, however, why *Urechis* should have a blood working at tensions as high as the trout, or the skate have a blood adapted to higher tensions, when temperature is taken into account, than the mackerel.

When the terrestrial vertebrates are considered, it is apparent that their bloods in general require higher oxygen tensions for half saturation. This fact is due in part no doubt to the higher temperatures at which these animals live, or maintain their body. At first sight one might expect the Amphibia and aquatic reptiles to have blood adapted to working at low tensions of oxygen, in a way similar to the carp and eel, yet this is clearly not the case. In order to properly weigh the data, it must be considered that the properties of the blood determine not only the conditions for the absorption of oxygen at the respiratory surface, but for its discharge from the blood into the tissues. Bloods with oxygen dissociation curves lying at low tensions favor the former and hinder the latter process. In each organism the optimal condition for the blood is a compromise in which these two processes are balanced. The factors determining the properties of the blood most favorable to the respiratory exchange are not only the tension of oxygen in the environment, but the structural and physiological properties of the respiratory organs and the vascular system as well as the general habits of the organism. The complex, and frequently antagonistic nature of these factors makes the teleological argument extremely dangerous, for it is easy to find some aspect of the problem for which the blood is well adapted, at the same time overlooking factors which may work the other way.

The tensions at which the bloods of the amphibians and terrestrial vertebrates combine with oxygen, when contrasted with the fishes, suggest an adaptation directed toward a more rapid and complete exchange of oxygen between the blood and the tissues. In the case of the aquatic reptiles, birds, and mammals, this may be an advantage in allowing the animal to utilize more completely the oxygen combined with the blood during periods when external respiration is interrupted by submergence. It is not clear how this would favor respiration in *Amphiuma*, which presumably absorbs oxygen from the water in which it is submerged. In the warm-blooded vertebrates, with their high metabolic rates, the high tension at which oxygen is held in the blood is of undoubted advantage in facilitating the rapid flow of oxygen from the blood to the tissues. In this way

the properties of the blood of the birds (81) and the sea lion (31) are of advantage.

A different interpretation of these facts has recently been developed (59) from the consideration that the properties of the blood may be related to the characteristics of the atmosphere at the time when the various forms were evolved, rather than to the nature of their present-day environment. If the view postulated by certain geologists, that the quantity of oxygen in the atmosphere has increased since the earlier Paleozoic times, be accepted, it is not unreasonable to expect that the more recent group of animals may possess blood capable of taking advantage of this change. With this view the data here under review are in general accordance.

The relations of carbon dioxide to the oxygen equilibrium are also important and complicate the appraisal of any argument concerning the adaptation of the bloods to respiratory needs. It has been pointed out that the transport of carbon dioxide is dependent in large measure upon the buffer action of hemoglobin and that in most animals the character of the carbon dioxide dissociation curve is related to the quantity of hemoglobin in the blood and hence to its oxygen-carrying power. This is appropriate, for in general the need for transporting carbon dioxide is proportional to the oxygen consumption.

The pressure of carbon dioxide in the blood varies greatly in different animals, depending largely on whether the respiratory organs are gills or lungs. In the case of the fish the blood is exposed to very low tensions of carbon dioxide in traversing the gills, and consequently contains carbon dioxide at pressures which do not appear to exceed a few millimeters (20) (65). The hydrogen ion concentration of the fish blood is consequently lower than that usually observed in other vertebrates. This fact alone tends to cause the blood to combine with oxygen at low tensions and, together with the temperature of the water, accounts in large part for the generally low range of oxygen pressures at which fish blood functions. These factors do not, of course, explain the different characters of the blood of different fishes. Root has pointed out the high sensitivity of the hemoglobin of certain teleosts to carbon dioxide and has suggested that it is adjusted to function in an environment of low carbon dioxide tension, such as the gills offer. This point is of importance in evaluating the properties of the blood of the higher vertebrates. One might equally well say that the blood of fishes is ill adapted to functioning under the higher carbon dioxide pressures to which the blood of all pulmonate vertebrates is exposed and thus stress the adaptive character of the latter.

It has been pointed out that the carbon dioxide dissociation curve of the blood of a number of the lower vertebrates is peculiarly high and flat, owing to the large quantity of bicarbonate present in it. It is difficult to see what purpose is served by this special arrangement, as it can be of no advantage in buffering the blood against carbonic acid. It would, however, enable the animal to care for the accumulation of considerable quantities of non-volatile acid through the elimination of an equivalent quantity of carbon dioxide. It is noteworthy that the animals possessing blood with this character are all fresh-water vertebrates whose habitats or habits submit them from time to time to asphyxial conditions. If this generalization is valid one might expect a similar type of carbon dioxide dissociation curve in the crocodile. This is not the case, however, in the blood of the

crocodile, of which the carbon dioxide dissociation curve is shown in Fig. 6. This blood contained a large quantity of lactic acid which may have decomposed the excess of bicarbonate. The high carbon dioxide capacities of the blood of the alligator observed by Hopping (38) when taken in connection with the accompanying oxygen capacities suggest that this animal also may have a carbon dioxide dissociation curve of the atypical form.

Arguments from the evolutionary and teleological viewpoints are equally treacherous and perhaps are not strictly pertinent to the scientific inquiry into the nature of the respiratory phenomena exhibited by the blood. It is safer and perhaps more valuable to inquire more closely into just what conditions characterize this function in the respiration of the living animal. There are sufficient data to define the conditions existing in the blood throughout the respiratory cycle in a number of animals and these are summarized in Table 7.

TABLE 7

Conditions Existing in the Blood in the Course of the Respiratory Cycle during Inactivity

SPECIES	URECHIS* (61)	SKATE (20)	SNAPPING TURTLE† (35)	DUCK‡ (81)	HORSE (35)	MAN (35)
Temperature, °C.	19	10.4	20	42	37	37
Oxygen capacity, vol. per cent.	4.50	6.00	6.40	17.0	21.4	20.5
Total O_2, vol. per cent:						
Arterial blood	4.1	5.90	5.82	16.6	20.0	19.4
Venous blood		1.98	2.12	6.6	13.5	14.1
Total O_2 transport		3.92	3.70	10.0	6.5	5.3
Saturation, per cent						
Arterial blood	97	93	95	95	98	96
Total CO_2, vol. per cent						
Arterial blood	8.8	7.70	96.43	47	44.9	48.2
Venous blood		10.84	99.39	55	50.3	52.0
Total CO_2 transport, vol. per cent		3.14	2.96	8	5.4	4.2
O_2 tension, mm. Hg						
Arterial blood	75	70	57.0	102	100	78
Venous blood		14	15.0	37	38	40
CO_2 tension, mm. Hg						
Arterial blood	7.2	1.3	38.5	54	41.6	40
Venous blood		2.6	45.2	65	49.2	45.4
CO_2 tension in respiratory organ	5.3	0				39
pH arterial serum	7.1	7.82	7.60		7.43	7.455
pH on becoming venous		−0.15	−0.06		−0.03	−0.026

* Conditions in coelomic fluid entered as arterial blood.

† Blood from lungs entered as arterial blood; blood from tissues entered as venous blood. For conditions in systemic arteries, see Henderson (35).

‡ Mean values from author's data.

In *Urechis*, a large worm of sedentary habit, there is no vascular system. The coelomic fluid, which functions as blood, has a relatively large volume and, although the erythrocytes are not numerous nor rich in hemoglobin, the total oxygen capacity is sufficient to last the animal for about an hour. One cannot distinguish between arterial and venous blood or properly speak of a circulation. The

coelomic fluid is merely churned about through peristaltic movements of the body wall and hind gut, successive portions of it being brought into contact with the active tissues or with the wall of the hind gut which forms the respiratory surface. The latter organ is "ventilated" with fresh water with sufficient regularity to keep more than a third of the oxygen within it from being absorbed. This gives sufficient oxygen pressure to saturate the blood almost completely and since only one-sixtieth of the blood's oxygen is used each minute, the blood as a whole remains so saturated. The coelomic fluid of *Urechis* serves as a reservoir for oxygen, keeping each tissue surrounded by an excessive supply of this gas, rather than as a means of bringing a constant stream of oxygen to the active parts. Carbon dioxide accumulates to a pressure of about five millimeters in the hind gut and consequently carbon dioxide is retained in the blood, but not at pressures greater than 7 millimeters. The coelomic fluid is unbuffered save for hemoglobin and consequently becomes more acid than sea water or the blood of higher forms but does not exceed neutrality.

In the skate anatomical considerations produce a situation in marked contrast. With the presence of a closed circulatory system the blood is concerned solely with *transport* of oxygen. The hemoglobin is well oxygenated in the gills, and in traversing the tissue capillaries gives up two-thirds of its oxygen content. This utilization, large when contrasted with the higher forms, implies a corresponding economy in the rate at which the blood is circulated and correlates with a circulatory system in which the blood must traverse two capillary systems in each circuit. Because of the high degree to which the oxygen is utilized, the pressure of oxygen in the venous blood, and presumably the mean pressure in the capillaries, is low. The pressure-head driving oxygen from blood to tissues must be correspondingly low, but this is tolerated because of the generally low metabolic rate of this inactive fish. In passing the gills the blood is exposed to water of negligible carbon dioxide content. The pressure of carbon dioxide in the blood and its carbon dioxide content are accordingly low and the pH value high. Corresponding to the large utilization of the oxygen in each increment of blood, there is an equally great carbon dioxide transport, relative to the total buffering capacity. The acid base equilibrium is shifted consequently as the arterial blood becomes venous and an unusually large change in pH of the blood results.

The snapping turtle resembles the skate in the fact that the utilization of oxygen is relatively great. In this form also the circulatory mechanism is spared at the expense of the oxygen-transporting power of the blood. The circulatory system is handicapped by the mixing of pulmonary and venous blood in the ventricle, so that the blood in the systemic circulation is not fully oxygenated and has characteristics midway between those listed as "arterial" and "venous" in Table 7. This fact must be important in necessitating the high utilization of the oxygen transport. The turtle's blood is well oxygenated when leaving the lung, although the pressure of oxygen in it is relatively low owing to the incompleteness in the ventilation of the lung. Because of the latter fact and the high degree to which the oxygen in the blood is utilized, the mean pressure of oxygen in the capillaries must be relatively low. The principal difference distinguishing the turtle from the fish consists in the high carbon dioxide tension in both arterial and venous blood, which is a reflection of the carbon dioxide accumu-

lated in the lung and the extraordinarily great total carbon dioxide content due to the atypical character of the carbon dioxide dissociation curve. These factors interact to give a pH value to the arterial blood which is higher than that found in the mammals though not so high as in the blood of the fish.

In the blood of the warm-blooded vertebrates the characteristics of the changes in the respiratory cycle reflect an organization suited to more intense metabolic activity. The oxygen capacity of the blood is much higher and the vascular system of these forms is suited to circulating the blood with greater rapidity and under higher pressure. In spite of the higher metabolic rates of the mammals, sufficient oxygen is supplied to the tissue without the utilization of such a large fraction of the oxygen contained in the blood, a possibility realized by virtue of the higher oxygen capacity and the more rapid rate of circulation. The pressure of oxygen in the venous blood and consequently the mean pressure existing in the capillaries, is maintained at a higher level than that observed in the cold-blooded forms. In this way a high pressure-head is provided for the rapid diffusion of oxygen from the blood to the tissues. The low degree of utilization of the oxygen present in the blood also leaves a larger margin which may be drawn on by the tissues during increased activity. The pressure of carbon dioxide in the blood is high since the ventilation of the mammalian lung is not sufficiently rapid to prevent the considerable accumulation of carbon dioxide in the alveolar air. The blood contains in consequence a high total carbon dioxide content, but as most of this is in the form of bicarbonate, it still retains a distinctly alkaline reaction. It is noteworthy that in the mammals the change in the pH in the blood passing from artery to vein is small compared to the lower forms, reflecting the higher development of the mechanisms for preserving the constancy of its physicochemical state.

The general picture presented by the blood of the duck differs from that observed in the mammals chiefly in the greater extent to which the oxygen circulating in the blood through the capillaries is utilized. It is difficult to be sure that this difference is not due to disturbances in the circulation or respiration incident to the collection of blood samples for analysis, since this was done, in the case of the data recorded for the duck, under anesthesia. However, the shape of the oxygen dissociation curve in the duck is such as to favor a high degree of utilization without corresponding loss in mean capillary oxygen pressure. It is not impossible that the high activities and metabolic rates of birds are facilitated by this character of the oxygen dissociation curve, enabling a greater quantity of oxygen to be transported by the blood and used without increasing the work which the heart must do in circulating the blood.

These cases make it clear that in the evolution of animals a wide variety has arisen in the quantitative aspects of the functioning of the blood in respiration. They depend on the specific properties as well as on the relative proportions of the constituents of the blood, and on the relations which exist between the activity of the animal, the nature of its environment, and the structure and function of its circulatory and respiratory mechanisms. On the whole, the picture is one of a system developing simultaneously in its various parts toward greater efficiency in supplying the requisites for activity, for terrestrial life, and for stability of function in the face of varying need.

In compiling the data presented in this paper it has been necessary frequently to change the units of measurement and carry out other minor mathematical transformations on the figures presented by the authors of the original work. For such changes the writer assumes full responsibility. References should consequently be taken as indicating the source from which the original information was obtained. In the citation of literature no attempt has been made at historical completeness and no attention has been paid to questions of priority as these matters are sufficiently presented in certain of the general papers referred to (1) (4) (5) (16) (30) (35) (64) (86). It has been the endeavor to draw attention rather to the principal recent investigations which contribute to the subject.

LIST OF LITERATURE

1. Anson, M. L., and Mirsky, A. E. 1930. Hemoglobin, the heme pigments, and cellular respiration. Physiol. Rev., Vol. X, p. 506.
2. Austin, J. H., Sunderman, F. W., and Camack, J. G. 1927. Studies in serum electrolytes. II. The electrolyte composition and the pH of serum of a poikilothermous animal at different temperatures. Jour. Biol. Chem., Vol. 72, p. 677.
3. Barcroft, Joseph. 1922. The raison d'être of the red corpuscle. Harvey Lectures, Series XVII, p. 146.
4. ———. 1925. The significance of hemoglobin in submammalian forms of life. Physiol. Rev., Vol. V, p. 596.
5. ———. 1928. The Respiratory Function of the Blood. Part II. Haemoglobin. Cambridge.
6. Barcroft, Joseph, and Barcroft, H. 1924. The blood pigment of Arenicola. Proc. Roy. Soc., London, B 96, p. 28.
7. Barcroft, J., and King, W. O. R. 1909. The effect of temperature on the dissociation curve of blood. Jour. Physiol., Vol. XXXIX, p. 374.
8. Baumberger, J. P., and Michaelis, L. 1931. The blood pigments of Urechis caupo. Biol. Bull., Vol. LXI, p. 417.
9. Boor, A. K., and Hektoen, L. 1930. Preparation and antigenic properties of carbonmonoxide hemoglobin. Jour. Infect. Dis., Vol. 46, p. 1.
10. Borden, M. A. 1931. A study of the respiration and of the function of haemoglobin in Planorbis corneus and Arenicola marina. Jour. Mar. Biol. Ass. Plymouth, Vol. 17, p. 709.
11. Brown, W. E. L., and Hill, A. V. 1923. The oxygen-dissociation curve of blood and its thermodynamical basis. Proc. Roy. Soc. London, B, Vol. 94, p. 297.
12. Chapheau, M. 1928. Recherches sur la respiration des hématies du siponcle. Bull. Sta. Biol. d'Arcachon, Vol. 25, p. 157.
13. Churchill, E. D., Nakazawa, F., and Drinker, C. K. 1927. The circulation of body fluids in the frog. Jour. Physiol., Vol. 63, p. 304.
14. Collip, J. B. 1921. The alkali reserve of the blood of certain of the lower vertebrates. Jour. Biol. Chem., Vol. 46, p. 57.
15. Cook, S. F. 1928. The action of potassium cyanide and potassium ferricyanide on certain respiratory pigments. Jour. Gen. Physiol., Vol. XI, p. 339.
16. Cuénot, L. 1891. Études sur le sang et les glandes lymphatiques dans la série animal. Arch. Zool. expér. et gén., 2 me Ser., T. IX, p. 366 and 593.

16a. Dawson, A. B. 1933. Supravital studies on the colored corpuscles of several marine investebrates. Biol. Bull., Vol. LXIV. In press.

17. Delaunay, H. 1913. Sur quelques faits particuliers à la répartition de l'azote dans le liquide cavitaire des vers (Aphrodite aculeata Sipunculus nudus). C. R. Soc. Biol., T. 74, p. 154.
18. Dill, D. B. Personal communication.
19. Dill, D. B., and Edwards, H. T. 1931. Physicochemical properties of crocodile blood (Crocodilus acutus, Cuvier). Jour. Biol. Chem., Vol. 90, p. 515.
20. Dill, D. B., Edwards, H. T., and Florkin, M. 1932. Properties of the blood of the skate (Raia ocellata). Biol. Bull., Vol. LXII, p. 23.
21. Dill, D. B., Edwards, H. T., Florkin, M., and Campbell, R. W. 1932. Properties of dog blood. Jour. Biol. Chem., Vol. 95, p. 143.
22. Dolk, H. E., and van der Paauw, F. 1929. Die Leistungen des Hämoglobins beim Regenwurm. Zeitschr. f. vergl. Physiol., Vol. 10, p. 324.
23. Drastich, L. 1928. Sur la concentration de l'hémoglobine dans les hématies nucléées et au cours de l'anémie chez l'homme. C. R. Soc. Biol., Paris, T. XCIX, p. 991.
24. ———. 1928. Ist die Konzentration des Blutfarbstoffes im Blutkörperchen bei allen Tieren konstant? Arch. ges. Physiol., Vol. CCXIX, p. 227.
25. Edwards, D. J. Personal communication.

26. Endres, G. 1930. Observations on certain physiological processes of the marmot, III, IV, and V. Proc. Roy. Soc. London, B, Vol. 107, p. 241.

27. Ferry, R. M., and Green, A. A. 1929. Studies in the chemistry of hemoglobin. III. The equilibrium between oxygen and hemoglobin and its relation to changing hydrogen ion activity. Jour. Biol. Chem., Vol. 81, p. 175.

28. Fischer, H. 1930. Hämin, Bilirubin und Porphyrine. Die Naturwissenschaften, Jahrg. 18, p. 1026.

29. Fischer, H., and Kirrmann, A. 1929. Synthesen von Mesoporphyrin, I, IV, XIII, and XIV. Liebig's Annalen der Chemie, Vol. 475, p. 266.

30. Fischer, H., and Treibs, A. 1930. Farbstoffe mit Pyrrolkernen. Handbuch der Biochemie des Menschen und der Tiere herausgegeben von C. Oppenheimer. Zweite Auflage, Erganzungsband, p. 72, Jena.

30a. Florkin, M. 1932. La courbe de dissociation de l'oxyhemerythrine dans le liquide coelomique du Siphoncle. Compt. Rend. Acad. Sci. Paris, Vol. 195, p. 832.

31. Florkin, M., and Redfield, A. C. 1931. On the respiratory function of the blood of the sea lion. Biol. Bull., Vol. LXI, p. 422.

32. Fox, H. M. 1926. Chlorocruorin: a pigment allied to haemoglobin. Proc. Roy. Soc., B, Vol. 99, p. 199.

32a. ———. 1932. Oxygen affinity of chlorocruorin. Proc. Roy. Soc., B, Vol. 111, p. 356.

32b. Green, Arda A., and Redfield, A. C. 1933. On the respiratory function of the blood of the porpoise. Biol. Bull., Vol. LXIV. In press.

32c. Green, Arda A., and Root, Raymond W. 1933. The equilibrium between hemoglobin and oxygen in the blood of certain fishes. Jour. Biol. Chem. In press.

33. Hall, F. G., and Gray, I. E. 1929. The hemoglobin concentration of the blood of marine fishes. Jour. Biol. Chem., Vol. 81, p. 589.

34. Haurowitz, F. 1929. Zur Chemie des Blutfarbstoffes. 10. Mitteilung. Über die Spezifität der Hämoglobine und die v. Krügersche Reaktion. Hoppe-Seyler's Zeitschrift f. physiol. Chem., Vol. 183, p. 78.

35. Henderson, L. J. 1928. Blood; a Study in General Physiology. New Haven. 397 pages.

36. Henderson, L. J., Dill, D. B., Edwards, H. T., and Morgan, W. O. P. 1930. Blood as a physicochemical system. X. The physicochemical properties of oxygenated human blood. Jour. Biol. Chem., Vol. 90, p. 697.

37. Hill, A. V. 1910. The possible effects of the aggregation of the molecules of haemoglobin on its dissociation curves. Jour. Physiol., Vol. XL, p. iv.

38. Hopping, A. 1923. Seasonal changes in the gases and sugar of the blood and the nitrogen distribution in the blood and urine of the alligator. Am. Jour. Physiol., Vol. 66, p. 145.

39. Hubrecht, A. A. W. 1875. Untersuchungen über Nemertinen aus dem Golf von Neapol. Niederlandisches Archiv für Zoologie, II, p. 99.

40. Jordan, H. E. 1931. The evolution of blood-forming tissue. Anat. Rec., Vol. 51, Suppl., p. 85.

41. Jordan, H. J. 1929. Allgemeine vergleichende Physiologie der Tiere. Berlin and Leipzig.

42. Jordan, H., and Schwartz, B. 1920. Einfache Apparate zur Gasanalyse und Mikrorespirometrie in bestimmten Gasgemischen, und über die Bedeutung des Hämoglobins beim Regenwurm. Arch. ges. Physiol., Vol. 185, p. 311.

43. Kawamoto, N. 1929. Physiological studies on the eel. I. The seasonal variation of the blood constituents. Sci. Rep., Tohoku Imp. Univ., Ser. 4, Biology, Vol. IV, No. 4, p. 635.

44. ———. 1929. Physiological studies on the eel. II. The influence of temperature and of the relative volumes of the red corpuscles and plasma upon the haemoglobin dissociation curve. Sci. Rep. Tohoku Imp. Univ., Ser. 4, Biology, Vol. IV, No. 4, p. 643.

45. Keighley, G. L. Personal communication.

46. Keilin, D. 1925. On cytochrome, a respiratory pigment, common to animals, yeast, and higher plants. Proc. Roy. Soc. London, B, Vol. 98, p. 312.

47. ———. 1929. Cytochrome and respiratory enzymes. Proc. Roy. Soc. London, B, Vol. 104, p. 206.

48. Kirrmann, A. 1930. Contribution à l'étude des hémoglobines. Le groupe prosthétique de l'hémoglobine de Chironome. Bull. Soc. Chim. biol., Vol. 12, p. 1146.

48a. Kobayashi, S. 1932. The spectral properties of hemoglobin in the holothurian, Caudina chilensis (J. Muller) and Molpadia roretzii (v. Marenzeller). Sci. Rept. Tohoku Imp. Univ., Ser. 4, Biology, Vol. VII, No. 2, p. 211.

49. Krogh, A., and Leitch, I. 1919. The respiratory function of the blood in fishes. Jour. Physiol., Vol. 52, p. 288.

50. Lankester, E. R. 1872. A contribution to the knowledge of hemoglobin. Proc. Roy. Soc. London, Vol. 21, p. 70.

51. Lankester, E. R. 1881. On Thalassema neptuni Gaertner. Zool. Anz., Vol. IV, p. 350.
52. Leitch, I. 1916. The function of haemoglobin in invertebrates with special reference to Planorbis and Chironomus larvae. Jour. Physiol., Vol. 50, p. 370.
52a. Lepkovsky, S. 1930. The serum and plasma proteins in fish. Jour. Biol. Chem., Vol. 85, p. 667.
53. Marrian, G. F. 1927. A note on haemerythrin. Brit. Jour. Exper. Biol., Vol. IV, p. 357.
54. Mendel, L. B., and Bradley, H. C. 1905. Experimental studies on the physiology of the mollusks. First paper. Am. Jour. Physiol., Vol. XIII, p. 17.
55. Miall, L. C. 1895. The Natural History of Aquatic Insects. London.
56. Moseley, H. N. 1874. On the anatomy and histology of the land-planarians of Ceylon, with some account of their habits, and a description of two new species, and with notes on the anatomy of some European aquatic species. Phil. Trans. Roy. Soc. London, Vol. 164, p. 105.
57. Ponder, E. 1924. The Erythrocyte and the Action of Simple Haemolysins. London.
58. Prenant, M. 1922. Recherches sur le parenchyme des plathelminthes. Arch. de Morph. gén. et expér., Vol. 5, p. 1–174.
59. Redfield, A. C. 1931. Quelques aspects du problème de l'évolution de la function respiratoire du sang. Revue des Questions scientifiques, p. 38.
60. ———. Not previously published.
61. Redfield, A. C., and Florkin, M. 1931. The respiratory function of the blood of Urechis caupo. Biol. Bull., Vol. LXI, p. 185.
62. Redfield, A. C., Humphreys, G., and Ingalls, E. 1929. The respiratory proteins of the blood. IV. The buffer action of hemocyanin in the blood of Limulus polyphemus. Jour. Biol. Chem., Vol. 82, p. 759.
63. Roche, J. 1930. Recherches sur la globine. C. R. des Trav. du Lab. Carlsberg, Vol. 18, No. 4, p. 1.
64. Romieu, M. 1923. Recherches histophysiologiques sur le sang et sur le corps cardiaque des annélides polychètes. Arch. de Morph. gén. et expér., fasc. 17, 339 pp., 7 pl.
65. Root, R. W. 1931. The respiratory function of the blood of marine fishes. Biol. Bull., Vol. LXI, p. 427.
66. Sato, T. 1931. Untersuchungen am Blut der gemeinen japanischen Archemuschel (Arca inflata). Zeitschr. f. vergl. Physiol., Vol. 14, p. 763.
67. Scott, W. J. 1931. Oxygen and carbon dioxide transport by the blood of the urodele, Amphiuma tridactyla. Biol. Bull., Vol. LXI, p. 211.
68. Smith, H. W. Personal communication.
69. ———. 1930. Metabolism of the lung-fish, Protopterus aethiopicus. Jour. Biol. Chem., Vol. 88, p. 97.
70. Southworth, F. C., and Redfield, A. C. 1926. The transport of gas by the blood of the turtle. Jour. Gen. Physiol., Vol. IX, p. 387.
70a. Sudzuki, M. 1924. Untersuchungen über Cetacea. VIII. Über das Blut. Tohoku Jour. Exper. Med., Vol. V, p. 419.
71. van der Lingen, J., and Hoogen, L. 1928. The perivisceral fluid of Cucumaria frauenfeldi. Trans. Roy. Soc. S. Africa, Vol. 16, p. 205.
72. Van Slyke, D. D. 1922. On the measurement of buffer values and on the relationship of buffer value to the dissociation constant of the buffer and the concentration and reaction of the buffer solution. Jour. Biol. Chem., Vol. 52, p. 525.
73. ———. 1926. Factors Affecting the Distribution of Electrolytes, Water, and Gases in the Animal Body. Philadelphia and London.
74. Van Slyke, D. D., Hastings, A. B., Heidelberger, M., and Neill, J. M. 1922. Studies of gas and electrolyte equilibria in the blood. III. The alkali-binding and buffer values of oxyhemoglobin and reduced hemoglobin. Jour. Biol. Chem., Vol. 54, p. 481.
75. Van Slyke, D. D., Hastings, A. B., and Neill, J. M. 1922. Studies of gas and electrolyte equilibria in the blood. IV. The effect of oxygenation and reduction on the bicarbonate content and buffer value of blood. Jour. Biol. Chem., Vol. 54, p. 507.
76. Van Slyke, D. D., Wu, H., and McLean, F. C. 1923. Studies of gas and electrolyte equilibria in the blood. V. Factors controlling the electrolyte and water distribution in the blood. Jour. Biol. Chem., Vol. 56, p. 765.
77. Van Slyke, D. D., Hastings, A. B., Hiller, A., and Sendroy, J. 1928. Studies of gas and electrolyte equilibria in blood. XIV. The amounts of alkali bound by serum albumin and globulin. Jour. Biol. Chem., Vol. 79, p. 769.
78. Warburg, O., and Christian, W. 1931. Über Phäohämin b. Biochem. Zeitschr., Vol. 235, p. 240.
79. Warburg, O., Negelein, E., and Haas, E. 1930. Spirographishämin. Biochem. Zeitschr., Vol. 227, p. 171.
80. Wastl, H. 1928. Beobachtungen über die Blutgase des Karpfenblutes. Biochem. Zeitschr., Vol. 197, p. 363.

81. Wastl, H., and Leiner, G. 1931. Beobachtungen über die Blutgase bei Vögeln. I. Mitteilung. Arch. ges. Physiol., Vol. 227, p. 367.

82. ———. 1931. Beobachtungen über die Blutgase bei Vögeln. II. Mitteilung. Arch. ges. Physiol., Vol. 227, p. 421.

83. ———. 1931. Beobachtungen über die Blutgase bei Vögeln. III. Mitteilung. Arch. ges. Physiol., Vol. 227, p. 460.

84. Wastl, H. A., and Seliškar, A. 1925. Observations on the combination of CO_2 in the blood of the bull frog (Rana catesbiana). Jour. Physiol., Vol. LX, p. 264.

85. Winterstein, H. 1909. Zur Kenntniss der Blutgase wirbelloser Seetiere. Biochem. Zeitschr., Vol. 19, p. 384.

86. ———. 1925. Handbuch der vergleichenden Physiologie. Band I, Hälfte I.

87. Wolvekamp, H. P. 1932. Untersuchungen über den Sauerstofftransport durch Blutpigmente bei Helix, Rana und Planorbis. Zeitschr. f. vergl. Physiol., Vol. 16, p. 1.

THE EVOLUTION OF BLOOD-FORMING TISSUES

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THE phylogeny of hemopoietic tissues may be traced in a direct line from lower invertebrates to mammals. The attempt accurately to plot this route becomes a fascinating exercise, and the data disclosed provide a highly interesting story. Whether the sequence suggested is closely authentic, as representing faithfully actual evolutionary events, may be considered doubtful at certain points, more especially at that which pertains to the transition from the achordata to the chordata. However, the larger features of the outline, particularly among the vertebrates, may be accepted confidently as substantially in accord with a reasonable interpretation of the facts. At any rate, no real hiatus exists as regards blood and blood-forming tissues between invertebrates and vertebrates. Whether the evolution of blood as between these two groups be regarded as continuous or parallel, the occurrence of erythrocytes and even erythroplastids in the blood of both certain worms and of mammals removes any basis for fundamental distinction in respect of blood. Moreover, lymphocytes and granulocytes, eosinophilic, special and basophilic, occur throughout the metazoa except the very lowest. Also, a peculiar type of spindle cell, a modified lymphocyte, occurs both in certain polychetes (e.g., *Amphitrite*) and in cyclostomes. There are no doubt many instances of parallelism in the evolutionary process. As such may be designated with considerable degree of certainty, the presence of erythrocytes in the annelid and echinoderm phyla; respiratory pigment in the blood plasma of Mollusca and Crustacea; lymphogenous organs in arachnids, Mollusca, Echinoidea and Aves; and the various types of granulocytes among certain classes.

For the purpose in hand it will be essential to adhere closely to what appears to be the main track of evolutionary advance. This may not at all points correspond with the accepted taxonomic order; data concerning blood forming tissues will be considered apart from other phylogenetic data. The temptation to digress along side lines, as among the Mollusca and the Arthropoda, must here be resisted in the interests of simplicity and appropriate space limitations. The direct line of blood evolution leads apparently at the crucial level from segmented worms to cyclostomes. Hematological data give comparatively little support to the hypothesis of the arachnid origin of vertebrates (Patten, '12). The blood of arachnids contains lymphocytes, monocytes, and eosinophils with bacillary granules; but it lacks cells with respiratory pigment. The presence of lymphogenous organs (e.g., the 'gland of Blanchard' in scorpions) suggests a high level of development, but apparently only signifies an instance of parallel evolution.

Respiratory pigment

Before passing to the consideration of blood cells, the location of respiratory pigments should be considered. Where such pigments occur, as among certain worms, holothurians, gastropods, Crustacea, and *Limulus*, whether in the form of hemoglobin, hemerythrin, chlorocruorin,

or hemocyanin, it resides generally in the celomic fluid or the blood plasma. In a few forms among certain worms it is located in cells, apparently modified lymphocytes. It would seem logical to conclude that residence of respiratory pigment in cells represents an evolutionary functional advance over its solution in the plasma. This is the generally accepted interpretation. However, certain facts disclosed by Redfield and Florkin ('31) demonstrate that inclusion of hemoglobin within cells does not among invertebrates necessarily signify a superior oxygen-carrying mechanism as compared with its solution in plasma. They have shown that the bloods of *Arenicola* and *Spirographis*, where the respiratory pigments, hemoglobin and chlorocruorin respectively, are carried in solution in the plasma, have a greater oxygen content than *Urechis* and the other invertebrate forms in which oxygen is transported in hemoglobiniferous cells.

BLOOD FORMING TISSUES OF INVERTEBRATES

Hemocytopoietic tissue makes its first appearance in the lower Metazoa. At the beginning, as exemplified by the sponges, it is represented by lymphocyte-like cells of larger and smaller varieties, and by granulocytes. These cells are ameboid elements within the mesoglea. The so-called lymphocytes have in general the characteristics of the hemocytoblasts of vertebrate forms. They are variously designated as hyaline leukocytes (Kollmann, '08) and amebocytes (Cuénot, '29). The granulocytes are weakly acidophilic. Only slight advance has been effected as far as the flatworms. The blood elements are still diffusely scattered through the middle body layer, except for the small number which have migrated into the primitive vascular system in the Nemertinea.

Beginning with segmented worms a tremendous evolution has been achieved. A series of segmentally arranged leukocytopoietic organs occurs. These organs produce granulocytes and lymphocytes. The hemocytopoietic tissue is the epithelium lining the peritoneal cavity. The arrangement is admirably illustrated in the case of the oligochete, *Pheretima indica*, recently studied by Kindred ('29). The 'blood' cells are essentially celomic elements. Secondarily these cells migrate in part into the blood vascular channels. The blood plasma of annelids contains a respiratory pigment, either hemoglobin or hemerythrin. Among the invertebrates the vascular channels develop independently of their cellular contents. Among the vertebrates also, vasculogenesis and hemocytogenesis are independent processes except in the Amniota during earliest stages, especially in the yolk sac. In the Anamniota the two processes are separate from the beginning. This matter will be discussed below.

In a few aberrant (degenerated or specialized?) annelids, namely the gephyreans and glycerids, blood-cell evolution has approached the limit achieved by the higher vertebrates. Hemoglobin-containing 'erythrocytes' occur (Goodrich, '97; Redfield and Florkin, '31); and in two genera, namely *Thallasema* and *Magelona*, even anucleation takes place (Romieu, '23), producing thus genuine erythroplastids, comparable to the red blood corpuscles of mammals. These erythrocytes are essentially modified lymphocytes. Nothing higher than this is achieved among invertebrates. Only in certain holothurians (e.g., *Thyone*, Van der Heyde, '22; *Cucumaria*, Kindred, '24) do a few hemoglobiniferous cells occur. Kindred suggests that the need for erythrocytes in these forms may be related to the presence of considerable muscle.

Among the Arthropoda and the Mollusca, the respiratory pigment of the blood plasma is hemocyanin, a copper-containing substance. Lymphogenous organs occur throughout these groups. The 'blood' cells are still essentially peritoneal elements. Secondarily they may enter the blood vessels. They include lymphocytes and granulocytes.

The earliest chordata show a decided retrogression, as compared especially with segmented worms. Only in the lowest fishes, the cylostomes, do we encounter a higher degree of development of hemocytopoietic tissue. In *Balanoglossus* and *Amphioxus* blood cells are represented only by a few very primitive amebocytes. The blood of tunicates contains in addition primitive amphophilic granulocytes and cells with variously colored spherules (George, '31).

The subvertebrate chordates, as regards hemocytopoietic tissue, are at about the level of the nemertean worms. If the blood-evolutionary process was continuous from invertebrates to vertebrates, it must apparently be traced from annelids to cyclostomes; and the intermediate groups of the taxonomic order must be considered as representing retrogressions or specialized side branches. All things considered, it seems more in accord with the data to consider blood evolution in vertebrates and invertebrates as a parallel than as a continuous process. However, no real gap exists between vertebrate and invertebrate bloods. Erythrocytes and even erythroplastids occur in both groups; and lymphocytes (hemoblasts; amebocytes) and granulocytes, with closely similar characteristics, occur from sponges to man.

Significance of blood

The primary purpose of blood is tissue respiration. This necessitates the transportation of oxygen. Accordingly, efficient blood must have oxygen-carrying capacity. Under the simple conditions in certain worms the celomic fluid subserves this function in slight degree. Where a simple vascular system has appeared the blood plasma assists or takes predominance in this function. The oxygen-carrying property of these fluids is enhanced by the presence of a respiratory pigment, like hemoglobin. A still more efficient respiratory mechanism is developed with the segregation of the respiratory pigment in certain cells, first of the celomic fluid, secondarily of the blood vessels. The cells available for this purpose are the primitive lymphoid hemoblasts. In annelids these are free peritoneal elements, circulating originally in the celomic fluid. In the vertebrates they are lymphocyte-like cells derived from the reticular stroma enveloping venous sinusoids, whether in spleen or bone marrow. The shift from exclusive splenic erythrocytogenesis to predominant bone-marrow erythrocytogenesis at the level of the Anura may mean largely a gain in bulk of hemopoietic tissue necessitated by an increasing degree of metabolic activity in the transition from cold to warm blooded animals. The shift was made readily possible by reason of the favorable vascular conditions of the marrow, in essential respects closely similar to those of the spleen. The initial purpose of blood vessels was apparently to permit a more intimate circulation of plasma. Cells were only secondarily added, by process of invasion. The vascular system furnishes a ready means for the wide and rapid distribution of granulocytes and phagocytes. At the level of the higher worms, the ancestral leukocytes (lymphoid hemoblasts) became utilized for the elaboration of respiratory pigment in the service of tissue respiration, in the form of erythrocytes.

BLOOD FORMING TISSUES OF VERTEBRATES

Confining further attention to the hemocytopoietic tissue of vertebrates, we encounter most primitive conditions in the hagfish (*Myxine glutinosa*). Among vertebrates the fundamental blood-producing tissue is the mesodermal envelope (submucosa) of the gastro-intestinal canal. In the hagfish this layer contains innumerable masses of actively hemocytopoietic tissue enveloping the venous channels in the form of islets and cords of differentiating blood cells (Jordan and Speidel, '30). This tissue constitutes in fact a disperse spleen (fig. 1). As such it represents the earliest known stage in the phylogeny of the spleen. The spleen is the primary blood-forming organ throughout the vertebrate group.

FIG. 1. TRANSVERSE SECTION OF PORTION OF INTESTINAL WALL OF HAGFISH, INCLUDING ONE LONGITUDINAL FOLD

The core of the fold and the subjacent portion of the tela submucosa show the large irregular patches of splenic (myeloid) tissue enveloping the venous channels. Magnification 25 diameters.

The constituent cells of this primitive

spleen are hemoblasts and granuloblasts. The walls of the venous sinusoids are fenestrated. Hemoblasts freely enter the sinusoids. Here the larger hemoblasts differentiate into erythrocytes; the smaller differentiate into spindle cells and thrombocytes. Granuloblasts begin their differentiation only extravascularly; the differentiation may be completed within the circulation. In the hagfish the general circulation is a locus of extensive blood cell proliferation and differentiation.

Conditions in the lamprey are very similar to those in the hagfish, except that a slight advance has been achieved in the evolution of the spleen. The spleen is still diffuse, but not disperse; it is still within the intestinal wall, but aggregated largely within the spiral valve (fig. 2). This hemocytopoietic tissue of the marsipobranchs has the essential characteristics of red bone-marrow. It is virtually myeloid tissue. This identity of splenic, myeloid and lymphoid tissue in the early stages of the evolution of hemocytopoietic tissue is of primary significance. The central fact in this evolutionary process concerns the phylogenetic history of the lymphocyte.

The Dipnoi present the third salient step in the evolution of the spleen (fig. 3). The spleen is still intraenteral, but it is now fairly sharply segregated in the wall of the stomach (Jordan and Speidel, '31). Granulocytopoiesis remains extensive and active in the wall of the intestine. This granulocytopoietic remnant of an originally disperse spleen within the wall of the intestine foreshadows the lymphoid aggregate nodules of the intestine of mammals. It represents further the first step in the future complete separation of the original tripartite condition of the primitive spleen into tissues essentially lymphocytopoi-

Fig. 2. Transverse Section of Intestine of Lamprey
The hemocytopoietic (splenic) tissue is aggregated in the spiral valve. Magnification 70 diameters

etic, granulocytopoietic and erythrocytopoietic.

In ganoids appears the earliest stage of the extraenteral spleen. Here the spleen is a compact, sharply segregated mass of hemocytopoietic tissue, close to the gastro-intestinal junction but topographically distinct and attached to the mesentery. In all of the higher vertebrates the spleen is essentially like that of the ganoids, but spatially somewhat less closely related to the stomach. Ganoids are further peculiar in the possession of a distinct lymphoid organ on the surface of the heart (Drzewina, '05).

Among vertebrates red-cell formation is associated with the presence of a spleen. The sub-vertebrate chordates lack both hemoglobiniferous cells and a spleen. Furthermore, erythrocytopoiesis is associated with a sinusoidal venous circulation. The special condition of a sluggish or relatively stagnant blood current provides the necessary stimulus for hemoglobin elaboration. The specific factor is presumably relatively high carbon dioxide concentration.

It would be expected theoretically that hemocytopoiesis should occur also in the mesonephros. This is actually the case. In ganoids renal hemocytopoiesis is quite

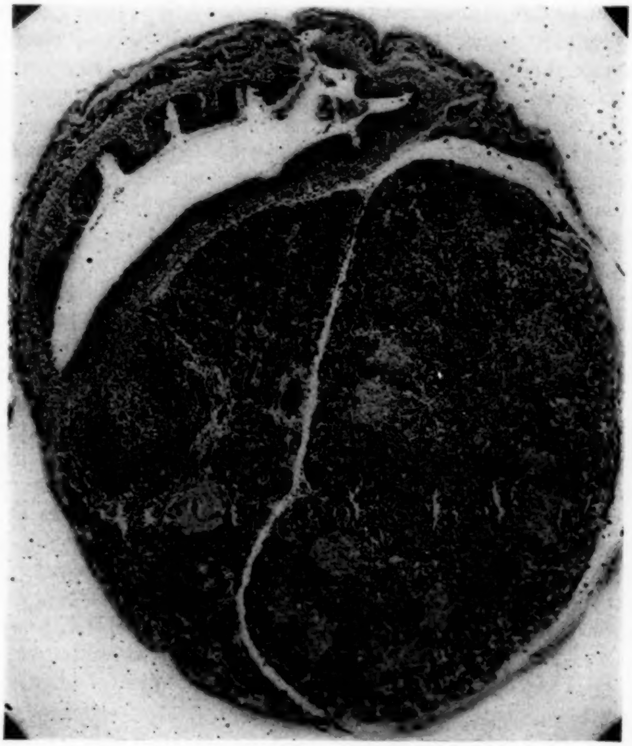

Fig. 3. Transverse Section of Stomach of African Lungfish

The spleen is embedded in the wall of the stomach. Between the gastric lumen (at left) and the spleen (at right) appears a portion of the pancreas. Magnification 70 diameters.

active, especially granulocytopoiesis. The same is true for elasmobranchs, and more especially for teleosts. It occurs also extensively in larval amphibians. The renal portal system provides the condition favorable for red-cell formation. The sinusoidal venous mechanism of the mesonephros is closely like that of spleen and bone-marrow. Granulocytes differentiate adjacent to the venous channels and subsequently penetrate their walls. Entering lymphoid hemoblasts differentiate into erythrocytes within the venous lumen.

In elasmobranchs a further division of the hemocytopoietic process occurs. Granulocytopoiesis is active in the subcapsular and stromal areas of the gonads. The mother tissue is a primitive connective tissue. This represents a special modification of the hemocytopoietic process in this group. It apparently has no evolutionary significance beyond the fact that sparsely vascularized mesenchyme is a potential locus for granulocytopoiesis.

A similar modification appears in most salamanders. Here granulocytopoiesis is largely restricted to the subcapsular (cortical) region of the liver. In *Proteus anginneus* it is restricted to the intertubular regions of the mesonephros. In *Necturus* this tissue occurs in considerable amount in both liver and mesonephros, and to a slight degree in the epicardium (Dawson, '32). The specific differential condition for granulocytopoiesis seems to be relatively sparse blood supply. The variable extraenteral distribution of loci of granulocytopoiesis in different classes, e.g., in gonads, mesonephroi, liver, bone marrow, appears to have little if any genetic significance. The selection of site for granulocyte differentiation seems to be a matter of adaptation to conditions peculiar to a class (e.g., elasmobranchs) or even a genus. In *Triturus* granulocytopoiesis is practically restricted to the subcapsular region of the liver. But in *Proteus*, conditions resemble those of teleost fishes; the liver is inactive or only slightly active and granulocytopoiesis is practically restricted to the mesonephros. However, in *Necturus* both liver and mesonephros are active. That hepatic granulocytopoietic activity is not closely related to the water-living habit, is indicated by the fact that in the terrestrial salamander, *Plethodon cinereus*, the liver contains a lymphogranulocytopoietic layer like that of *Triturus* and *Amphiuma*.

Hemopoietic conditions in *Proteus anguineus* merit further comment by reason of certain special characteristics. In the first place, lymphocytes are completely absent from the wall of the intestine; lymphocytes are not here lost by migration through the intestinal mucosa. The evidence is exceptionally clear that lymphocytes are lost by transformation into other types of blood cells. In the spleen the larger lymphocytes differentiate only into erythrocytes, the smaller into thrombocytes. Size of cell, or the stage of the distance in terms of number of mitoses from the ancestral lymphoid hemoblast seems to determine whether a cell shall develop hemoglobin and become an erythrocyte or develop thrombogenetic granules and become a thrombocyte. Similarly, in the mesonephros the newly-formed and larger lymphoid hemoblasts develop into eosinophils, the slightly smaller daughter cells of original hemoblasts develop into neutrophils. The evidence from *Proteus* is entirely in accord with the monophyletic theory of blood-cell origin.

In Amphibia we meet with the first appearance of hemocytopoietic bone marrow. In the Anura, as represented by the frog, the marrow of the long bones becomes very active in blood formation during metamorphosis, and annually for a brief period immediately following hi-

bernation. At other times red-cell formation is almost entirely restricted to the spleen. Lymphocytopoiesis is active in the intestine. In the Anura the small, diffuse collections of lymphocytes in the axillary and inguinal regions may foreshadow the future lymph nodes of higher vertebrates. Lymph nodes occur first in birds, and here only in water birds (Further, '13). They consist of two pairs of nodes, one in the neck and one near the kidneys. They are peculiar in that the more compact lymphoid tissue occurs centrally. Typical lymph nodes occur first in Mammalia.

Beginning with Reptilia, the bone marrow assumes a larger rôle in red-cell formation. The spleen remains active, but in lesser degree as we pass through Aves and the lower Mammalia. Among the Mammalia the spleen maintains a considerable adult activity in the opossum, the bat and the hedgehog.

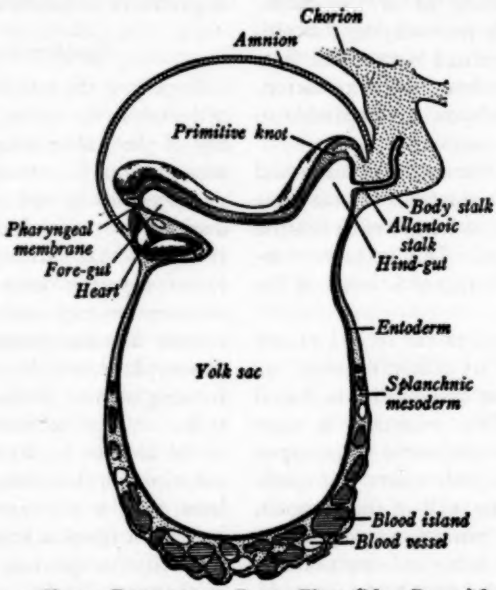

FIG. 4. RECONSTRUCTION OF A HUMAN EMBRYO OF THE FOURTH WEEK (MALL-DANDY) SEEN IN SAGITTAL SECTION After Prentiss and Arey. Magnification 23 diameters

HEMOPOIETIC SEQUENCE IN MAN

Before considering the significance of bone marrow hemocytopoiesis, it seems profitable to compare the ontogenetic history of blood-forming tissues in mammals with the phylogeny just outlined. The first locus of hemocytogenesis in the mammal is the wall of the yolk sac. Immediately after the first appearance of blood islands in the yolk sac, in part coincident with the process in this region, similar hemocytopoietic islands appear in the body stalk of primates. Next, such islands may appear in the body mesenchyme, then in the hepatic stroma. These regions remain active into the early part of the second month of embryonic development.

The hemocytopoietic loci mentioned represent in essence parts of the embryonic gut (fig. 4). This ontogenetic stage of hemocytopoiesis, covering approximately the first five weeks of human development,

corresponds roughly with the phylogenetic stage represented by the cyclostomes, when the spleen occurs as a disperse intraenteral organ. The gut arises from the vault of the primitive yolk sac. Following the partial separation of the gut from the yolk sac, the latter represents in essence a herniated portion of the intestine. The mesodermal body stalk covers the allantois, an evagination from the yolk sac or gut, thus in essence comparable to the mesodermal covering of the intestine. The primitive body mesenchyme also represents a peri-intestinal layer. The liver primordium is an intestinal evagination; its stromal mesenchyme is comparable to the intestinal submucosa.

For a time after the middle of the second month the hepatic sinusoids of man are a locus of extensive red cell multiplication and differentiation. This stage is comparable to the phylogenetic stage of the teleost fishes.

Towards the end of the second month the spleen begins its hemocytopoietic activity. The spleen develops in the dorsal mesogastrium. This condition is comparable to the phylogenetic stage represented by the lungfish where the spleen remains within the wall of the stomach. The spleen is the predominant erythrocytopoietic organ in fishes and amphibians.

Early in the third month of human development considerable hemocytopoiesis occurs in the mesonephros. Red cells differentiate within the venous channels; granulocytes differentiate extravascularly. In higher fishes and in larval Amphibia, the kidney has a variable but generally considerable hemocytopoietic activity. During the second and third months red cell proliferation and differentiation occur extensively also in the peripheral blood stream. This phase is comparable to similar activity in adult fishes and urodele Amphibia.

Bone marrow makes its appearance in man first during the sixth week, in the clavicles. During the third month bone marrow hemocytopoiesis is active. This stage is comparable to that represented in successively greater degree by reptiles, birds, and mammals.

Lymph nodes appear late in the third month. This ontogenetic stage corresponds with that represented by water birds, where for the first time two pairs of primitive nodes occur.

Significance of spleen

Regarding the spleen as an aggregation of lymphocytes in the mesodermal covering of the gastro-intestinal tract (dorsal mesogastrium), secondarily separated phylogenetically and ontogenetically as a distinct body attached to the mesentery, it appears that this organ is the primary hemocytopoietic tissue. Such interpretation requires explanation of secondary extensive hemocytopoietic activity in the mesonephros, and the predominant blood-forming activity of bone marrow in mammals. It requires further an explanation of the division in phylogeny of the original tripartite function of the spleen, among bone marrow and lymph nodes, with retention of lymphocytopoiesis and the potentiality to produce granulocytes and erythrocytes under certain conditions. The explanation may regard the lymphoid masses of the intestine as phylogenetic remnants of the originally intraenterally placed spleen, retained for purposes in part of supplying ancestors for granulocytes required presumably for antitoxic functions.

It needs to be emphasized that genuine lymphocytes occur in phylogeny long before lymph nodes appear. Genuine lymphocytes occur with the appearance of an aggregate spleen, accordingly first in the lungfish, more abundantly in ganoid and teleost fishes. Their evolu-

tion traces back to the hemocytoblasts of the cyclostome spleen.

The claim of Alder and Huber ('23) that lymphocytes occur for the first time in birds is based upon their failure to differentiate in the blood of amphibians and reptiles between the hemocytoblast and the lymphocyte stages of the lymphoid hemoblast. The hemocytoblasts are in general larger cells with more vesicular nucleus, the chromatin of which occurs in the form of minute granules evenly distributed. The lymphocytes are smaller cells, representing in general division products of hemocytoblasts. Their chromatin occurs in large irregular blocks. The nucleus of both hemocytoblasts and lymphocytes may contain one or several nucleoli. Between the two varieties of lymphoid hemoblasts occur transitional stages with respect to both cell size and nuclear configuration. Since lymphocytes were observed to differentiate into erythrocytes in the blood of amphibians and reptiles, Alder and Huber designated these cells hemocytoblasts. Such interpretation brings the matter in accord with the diphyletic theory of blood-cell origin, but it disregards the true morphology of the red-cell ancestor. The blood of amphibians contains both genuine hemocytoblasts and genuine lymphocytes. But the lymphocytes only represent later stages of differentiation of the hemocytoblasts and develop into erythrocytes in the splenic sinuses and in the circulation.

The essential features of the spleen as concerns red cell formation include lymphocytes and a sinusoidal venous circulation. The lymphocytes, as potential hemocytoblasts, develop into erythrocytes intravascularly, into granulocytes extravascularly. The sinusoidal circulation of the spleen is closely reproduced in liver, mesonephros and bone marrow. Hemocytoblasts (lymphocytes) in any of these locations differentiate into erythrocytes. The combination in these loci of the two fundamental requisite factors for red cell formation, lymphoid hemoblasts and stagnant blood, explains the hemocytopoietic activity.

Significance of bone marrow

Bone marrow arose as a necessary nutritive mechanism for hollow bones. Having the peculiar vascular arrangement requisite for hemocytopoiesis, circulatory hemoblasts aggregate here to further differentiate into erythrocytes. Since the stroma of bone marrow consists of reticular connective tissue, a local source of lymphocytopoiesis is provided. Lymphoid hemoblasts of bone marrow differentiate into granulocytes extravascularly and into erythrocytes intravascularly. Bone marrow hemocytopoiesis is thus, phylogenetically considered, in a sense an accidental matter, incidental to bone development.

Significance of lymph nodes

Can a similar interpretation be placed upon lymph nodes? The answer involves explanation of the function of lymph nodes. The obvious function of lymph nodes is the production of lymphocytes. But this is also a primary function of the spleen, and a partial function of bone marrow. It is clear also that lymph nodes serve as filters on the blood system. Lymph nodes, accordingly, function as accessory blood filters, removing certain deleterious products from the lymph before its mixture with the blood. Moreover, spleen and lymph nodes have an identical reticular stroma, the original source of lymphocytes and macrophages. Only the internal blood and lymph vascular systems are different in spleen and lymph nodes. In the spleen, due to the venous sinusoids, conditions are favorable for red-cell differentiation. Vascular conditions in

lymph nodes normally are unfavorable for such differentiation. Abnormally, as in certain leukemias and anemias, red cell formation may occur in lymph nodes; and granulocytes may arise from lymphocytes both in spleen and lymph nodes.

Lymph nodes, then, would seem to be in a sense accessory spleens, as concerns filtration and lymphocyte and macrophage production. They produce enormous numbers of lymphocytes daily. These lymphocytes enter the blood stream through the large lymphatic ducts. They represent circulatory hemocytoblasts, retaining potentialities for differentiation into erythrocytes, monocytes and granulocytes, depending upon specific environmental stimuli. Aggregating in bone marrow they encounter the proper stimuli leading to erythrocyte differentiation.

Significance of the thymus

The foregoing discussion has included no mention of the thymus. The omission is deliberate and seems warranted in view of the continued disagreement regarding the nature of the parenchyma. If the parenchyma is properly regarded as composed of lymphocytes, then the thymus belongs with the lymphoid organs. As such it is a lymphocyte producer. The local granulocytes are at least in large part immigrant elements. Since the thymus occurs throughout the vertebrate phylum it antedates lymph nodes, and may be regarded as accessory to the spleen in the production of lymphocytes.

THE EVOLUTION OF THE LYMPHOCYTE

The above discussion has involved in fact the evolution of the lymphocyte. Recapitulating this as a distinct subject, we must begin consideration with conditions in the hagfish. Here only lymphoid cells with typical hemocytoblast features occur. Extravascularly these differentiate into granulocytes, intravascularly into erythrocytes, thrombocytes and peculiar fusiform cells. The same is true for the lamprey. Thrombocytes and fusiform cells generally develop only from the smaller hemoblasts.

In the lungfish both typical hemocytoblasts and typical lymphocytes occur in the peripheral blood. Both undergo further differentiation, the larger into erythrocytes, the smaller into thrombocytes. The smallest lymphocytes, with pycnotic nuclei, in both the spleen and the circulation are apparently regressive phases and suffer degeneration. The term ***lymphoid hemoblast*** is used to designate inclusively hemocytoblasts and the hemogenic lymphocytes.

In ganoid and elasmobranch fishes lymphocytes begin to outnumber the hemocytoblasts in the circulation. The lymphocyte preponderance becomes still greater in teleost fishes. Circulatory hemocytoblasts become successively less numerous through the ascending scale of Urodela, Anura, and Reptilia. The blood of birds and mammals normally contains no hemocytoblasts. These cells are restricted to the central tissues; bone marrow, spleen and lymph nodes.

The lymphocyte represents a slightly more differentiated hemocytoblast. Small lymphocytes are the division products of large lymphocytes. Small lymphocytes may grow to become large lymphocytes. Lymphocytes, except the smallest which degenerate, maintain their ancestral hemocytoblast potentialities to differentiate into granulocytes and erythrocytes. The line of differentiation depends upon the specific environmental stimulus. Apparently, the smaller lymphocytes are produced for the purpose of ready transportation by the blood stream. They are filtered out in large numbers in the bone marrow where they presumably differentiate largely

into erythrocytes. Thus, the venous sinusoids of the bone marrow in the higher vertebrates would seem to subserve the same function as concerns red cell differentiation as does the general circulation in cyclostomes and lungfish and in the mammalian embryo. The lymphocyte, as a blood cell ancestor, has itself undergone evolution during vertebrate phylogeny. The essence of this evolutionary process concerns reduction in size, the results partly of nuclear concentration. The circulating thrombocytes of submammalian vertebrates are the homologues of the stationary megakaryocytes of the bone marrow of mammals.

The phylogenetic source of lymphocytes is the spleen. When lymph nodes become numerous and widely distributed, as in mammals, their lymphocyte products enter the blood stream and aggregate in bone marrow, where the conditions for erythrocyte differentiation are most favorable. The explanation of the origin of lymph nodes, in addition to a spleen, may pertain to their function as phagocyte (monocyte) producers. There is an obvious protective advantage in having these accessory spleens (lymph nodes) widely scattered. These excess lymphocytes may presumably perform their originally splenic function as erythrocyte producers in the bone marrow. Another advantage in the possession of lymph nodes and bone marrow, in addition to a spleen, may inhere in the greater flexibility of such a tripartite mechanism, with the resulting accession of factors of safety in the hemocytopoietic process, and the possibility of compensatory activity for subnormal conditions in any part of the system.

RELATION OF HEMOGENESIS TO VASCULOGENESIS

In young amphibian larvae the future blood-forming tissue is apparently sharply localized, in the form of a 'primitive blood island' in the mid-ventral region of the body between the liver primordium and the anal area. This 'island' has the form of an irregular V-shaped band of cells occupying a space between the entoderm and the ventral splanchnic mesoderm. It becomes visible macroscopically as a darker zone at the stage of development just prior to the beginning of heart pulsation. Frederici ('26) showed that excision of this blood island in embryos of *Rana fusca*, in no way interfered with the normal development of the vascular system; but such embryos lacked red blood cells. These results were confirmed by Goss ('28) for embryos of *Amblystoma punctatum*. Slonimski ('31) has repeated and extended these experiments with embryos of *Rana*, *Amblystoma* and *Bufo*. His results agree with those of Frederici and Goss: The mid-ventral blood island is the sole source of erythrocytes in the amphibian embryo; blood vessels and red blood cells have a different origin; erythrocytes do not arise from endothelium.

This larval blood island of amphibians obviously represents a specialized portion of the primitive submucosa of the gut. As such it is comparable to the spleen of the hagfish. If this comparison is legitimate, then excision of this primordium would necessarily remove all possibility of future development of the spleen and the differentiation of erythrocytes. Independence between vasculogenesis and hemocytogenesis prevails throughout the Metazoa, except in the early embryonic stages of the Amniota. Here, according to the current descriptions, endothelium arises from the peripheral cells of the yolk-sac blood islands, erythrocytes from the central cells. This exception may signify a specialization correlated with an extra-embryonic vascular area associated with a yolk sac. Within the embryonic

body itself, at least after the very earliest stages, vasculogenesis and hemocytogenesis, as in spleen and bone marrow, are again independent processes.

Since the blood vessels of the operated amphibian larvae contain leukocytes, explained as invasions from mesenchymal sources, Slonimski concludes that lymphocytes do not possess the capacity for erythrocyte differentiation; and he rejects the monophyletic interpretation of blood-cell development. However, removal of the primary source of larval erythrocytes, the primitive blood island, may interfere with the respiratory and metabolic needs of the embryo to such a degree as to render impossible the differentiation of lymphocytes into erythrocytes, known to occur in the circulation under normal conditions even in adult stages. Moreover, it must be pointed out that the operated embryos could not be kept alive much beyond a month. If the operated specimens could have been carried beyond the stage of spleen development, assuming that the spleen could differentiate under the conditions of lack of red blood cells even if its primordium had not been removed with the excision of the primitive blood island, the erythrocytopoietic capacity of the splenic lymphocytes might have been able to gain expression. Apparently then, the primitive blood island of amphibians is the sole source of the primitive line of red blood cells. Embryos deprived of this blood-cell primordium are incapable of survival to the time when a differentiated spleen could contribute a second line of erythrocytes and continue as a source for red cell ancestors, namely lymphoid hemoblasts.

SIGNIFICANCE OF RESULTS OF SPLENECTOMY

Splenectomy experiments with amphibia give supplementary information bearing on the phylogenetic sequence of hemocytopoietic tissue. Ablation of the spleen in larval urodeles results in regeneration (Drzewina, '05). In adult urodeles splenectomy results only in shifting erythrocytopoiesis to the general circulation (Jordan and Speidel, '30). Apparently, in the adult the perisplenic mesenchyme is too highly differentiated to serve as potential spleen primordium. In the Anura the results of spleen excision are variable. Frogs either die at about the sixtieth day after splenectomy or they live indefinitely. Those that live have compensated for the loss of the spleen in any one of four different ways. Some produce a new spleen. This result, in the light of conditions in the adult urodeles, must probably be interpreted as a hyperplasia of a microscopic accessory spleen. Some splenectomized frogs develop a hyperplastic marrow in the long bones. This may be interpreted as representing an obligatory utilization of a relatively less favorable, but potentially satisfactory available locus for blood formation. It is comparable to the shift made in evolution at the level of amphibians from splenic to bone marrow erythrocytopoiesis.

Some of the splenectomized frogs compensate by myeloid hyperplasia of the intertubular renal tissue. This represents a backward shift to an ontogenetic larval condition and to a phylogenetic ichthyoid condition. A few of the splenectomized frogs compensate only by myeloid metaplasia of the fat bodies. This result has apparently no phylogenetic significance; it represents utilization of a highly vascularized, structurally potentially favorable, locus for blood cell formation under extreme conditions.

SIMILARITIES OF VASCULAR ARRANGEMENT IN SPLEEN AND BONE MARROW

It may again be recalled that the spleen is the fundamental blood-forming organ in vertebrates. Utilization of bone marrow

is a secondary condition. Possibility of utilization of bone marrow for red cell production inheres in its peculiar vascular mechanism. While developed presumably for optimal bone nutrition, the essential conformity of this vascular mechanism to that of the spleen, made it at once available for the additional function of blood-cell differentiation. The very close similarity in the vascular mechanism of the spleen, from its most primitive condition in the hagfish to its most highly developed form in man, and to that of bone marrow where found, seems of primary significance. The essential matter concerns a structural condition producing a relative blood stasis. The essential structural details concern a rich plexus of venous sinusoidal channels, connecting proximally with long, narrow, non-anastomosing arterial capillaries. The resulting sluggish circulation within the sinusoids is further enhanced by the presence of openings in the endothelial lining providing numerous connections between the vascular lumen and the interstitial spaces of the reticular stroma. The fenestra permit of the ready entrance into the blood stream of extravascular granulocytes and lymphoid hemoblasts. The latter differentiate into erythrocytes within the venous sinuses. In the elaboration of hemoglobin a relatively high carbon dioxide tension is apparently of prime importance.

The splenic vascular arrangement is essentially identical from cyclostomes to mammals. In the hagfish long, straight, narrow capillaries pass from the external surface of the submucosa as branches from longitudinal vessels to the crest of the longitudinal mucous folds. Here they break into sprays of venous vessels which pass in the opposite direction to connect with deep longitudinal submucous veins. Only the venous portions of the vascular mechanism are enveloped with myeloid tissue. This consists of hemocytoblasts and differentiating granulocytes. Both enter the sinusoids for distribution throughout the vascular system. The hemocytoblasts differentiate intravascularly into erythrocytes, spindle cells and thrombocytes. The granulocytes begin their differentiation only extravascularly; the differentiation may be completed within the blood channels.

Conditions in the lamprey are essentially similar. In the spleen of the lungfish, located in the stomach wall, conditions are also closely similar except that granulocyte formation is more active. However, here we have the beginning of the separation of granulocytopoiesis and erythrocytopoiesis. Erythrocytopoiesis occurs only in the spleen; granulocytopoiesis occurs also in the submucosa of the gut throughout its entire extent. At higher levels the separation is maintained, until erythrocytopoiesis and granulocytopoiesis are again associated in the bone marrow of reptiles, birds and mammals. But even here the gut wall maintains considerable lymphocytopoietic and granulocytopoietic activity. The spleen retains practically only lymphocytopoietic activity. The most peculiar form of separation occurs in elasmobranchs where granulocytopoiesis occurs in the gonads; and in urodeles where it occurs in the periphery of the liver (e.g., *Triton*, *Amphiuma*) or in the intertubular stroma of the mesonephros, (e.g., *Proteus*, *Necturus*). All the regions of granulocytopoiesis are characterized by a relatively sparse vascularization.

In the highly developed spleen of mammals the peculiar vascular arrangement seen in cyclostomes is maintained. The nodular arterioles break up into postnodular branches long, straight, nonanastomosing arterioles and arterial capillaries (the sheathed arteries, or penicilli of Ruysch) which connect with a rich

plexus of venous sinusoids with fenestrated walls. This provides for the exit of senile reds and the admission of newly-formed lymphocytes. The lymphocytes do not normally, after post-fetal life, differentiate into erythrocytes within the circulation. Under certain pathological conditions, however, the spleen may revert to its fetal erythrocytopoietic activity. It appears quite possible that these lymphocytes may be filtered out into the sinuses of the bone marrow in part to differentiate into red cells. At any rate the bone marrow has the essential splenic vascular mechanism; one presumably especially adapted for red cell development. The marrow also is

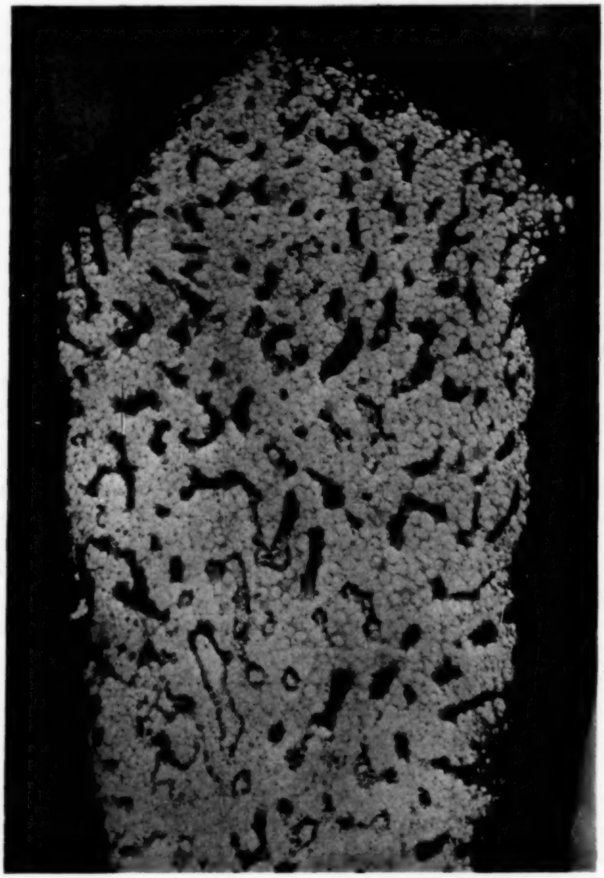

Fig. 5. Photomicrograph of Median Longitudinal Section of Femur of a Frog (Rana Pipiens), Showing the Usual Hypoplastic Conditions of the Marrow, an Extensively Vascularized Adipose Tissue

Only the venous sinusoids, some filled with blood, can be seen. Hemocytopoetic activity, exclusively granulocytopoetic, is practically limited to the epiphyseal borders and a very narrow discontinuous endosteal area. Magnification, 20 diameters.

characterized by long, straight, non-anastomosing arterial capillaries, which connect with an abundant venous sinusoidal mechanism. This is especially clearly seen in the normally hypoplastic marrow of the femur of the frog (figs. 5 and 6). Here, again closely recalling conditions in the primitive myeloïd spleen of hagfish, the venous channels in slightly hypoplastic marrow are ensheathed with differentiating granulocytes, and typical hemoblasts. Within the sinusoids the hemoblasts, passing through a lymphocyte stage, develop into erythrocytes and spindle cells. The differentiation of lymphoid hemoblasts into erythrocytes in the sluggish circulation in the avian and mammalian spleen and in the bone marrow is closely comparable to this process in the general circulation of fishes and amphibia.

Conclusions

The phylogenetic history of blood-forming tissues clearly indicates the primary importance of the spleen. Renal and bone marrow erythrocytopoiesis are secondary adaptations. The phylogenetic history further demonstrates the erythrocytogenic potentiality of the lymphocyte. The lymphocyte is a later stage of the hemocytoblast; as such it maintains the capacity for elaborating hemoglobin.

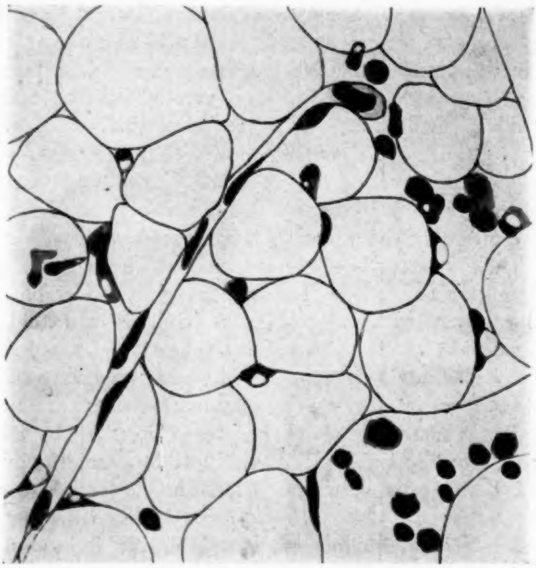

Fig. 6. Small Area of Femoral Marrow (Fig. 5), Showing a Long Arterial (Transition) Capillary to Left of Center; and a Venous Sinusoid with Lymphoid Hemoblasts at Right Lower Portion
From Jordan and Baker, Anat. Rec., vol. 35, 1927. Magnification, 500 diameters

SUMMARY

The direct phylogeny of the blood-forming tissues is obscured by many probable instances of parallel evolution. The less doubtful of these instances may include the elaboration of respiratory pigments among several classes of the invertebrates and all of the vertebrates; the occurrence of lymphogenous organs in segmented worms, gastropods, Crustacea, arachnids

and higher vertebrates; and the presence of similar varieties of granulocytes among the Achordata and the Chordata.

Assuming that the largest number of corresponding features indicates relatively more accurately the direct line of development, the transition from invertebrates to vertebrates, as regards hemogenic tissue, appears to have been made from annelids to cyclostomes. The blood of certain polychetes (e.g., *Amphitrite*) contains peculiar spindle cells, representing morphologically modified lymphocytes. Similar fusiform lymphocytes are found among the vertebrates only in the blood of hagfish and lampreys.

The celomic fluid of gephyreans and glycerids, peculiar worm-like forms generally interpreted as modified annelids, contains genuine erythrocytes similar to those of the blood of vertebrates; and several echiuroid genera (*Thallasema*, *Magelona*) have actual erythroplastids very like the red blood corpuscles of mammals.

Whether the evolution of hemocytopoietic tissue proceeded directly from invertebrates to vertebrates or not, there exists no real gap between the bloods of these larger groups. Apparently identical highly specialized blood cells occur in both groups.

Throughout these groups a lymphocyte-like cell represents the primordial element from which differentiate erythrocytes, granulocytes and monocytes. This primorial blood-cell is originally a peritoneal derivative and constitutes a portion of the cellular content of the celomic fluid. Secondarily, the lymphocytes and their differentiation products may migrate into the primitive vascular channels.

Among the vertebrates this primordial lymphoid hemoblast arises from mesoderm whether in yolk sac, spleen, lymph nodes or bone marrow. Here also in the special blood-forming organs, the spleen and bone marrow, it only becomes a vascular element following migration. Within the venous sinuses it may become transformed into erythrocytes and thrombocytes. Extravascular differentiation leads only to granulocytes; these cells pass through the fenestrated walls of the sinuses at various stages of development.

Beginning with the lowest vertebrates, the hagfish, the evolution of hemocytopoietic tissues presents a relatively clear picture. It involves primarily the spleen as the fundamental blood-forming organ.

In the hagfish the spleen consists of a diffusely scattered, perivenous myeloid tissue throughout the submucosa of the gastro-intestinal tract. In the lamprey the spleen is aggregated within the spiral valve. In the lungfish the spleen is still intraenteral, but no longer diffuse; it has become segregated within the wall of the stomach. The submucosa of the intestine retains considerable granulocytopoietic activity. In ganoid fishes the spleen is a sharply segregated extraenteral myeloid organ attached to the mesentery. In elasmobranchs and teleosts and all of the higher classes the spleen exists essentially as in ganoids. In Amphibia it is still the essential erythrocytopoietic organ. In certain fishes and in larval Amphibia the intertubular tissue of the mesonephros has accessory erythrocytopoietic function.

With the development of long hollow bones, beginning with the Anura, the spleen becomes increasingly less important as an erythrocytopoietic organ. In Aves and Mammalia it is substantially a vestigial organ; blood-formation is here restricted to the bone marrow. The substitution in evolution of bone marrow for spleen as the locus of blood formation finds its explanation in the peculiar vascular mechanism of marrow, and in the relatively larger area and more elastic na-

ture of this tissue. The essential identity between the vascular arrangement of the spleen and bone marrow inheres in the presence of long, straight, non-anastomosing arterial capillaries leading to an extensive system of venous sinusoids. The essential factors for hemoglobin elaboration in these sinusoids are relatively static blood and the consequent high carbon dioxide tension.

LIST OF LITERATURE

(1) Alder, A., and Huber, E. 1923. Untersuchungen ueber Blutzellen und Zellbildung bei Amphibien und Reptilien. Folia Haematologica, Bd. 29, S. 1–22.

(2) Cuénot, L. 1897. Les globules sanguins et les organes lymphoïdes des Invertébrés. Arch. Anat. Micr., vol. 1.

(3) Dawson, A. B. 1932. Hemocytopoietic loci in Necturus maculosa. Anat. Rec., vol. 52, pp. 367–380.

(4) Drzewina, A. 1905. Contribution à l'étude du tissue lymphoïde des Ichthyopsides. Arch. de Zool. Exp. et Gén., sér. 4, T. 3, p. 145.

(5) Frederici, E. 1926. Recherches expérimentales sur les potentialités de l'ilot sanguin chez l'embryon de Rana fusca. Arch. de Biol., T. 36, pp. 466–487.

(6) Further, H. 1913 Beiträge zur Kenntniss der Vogellymphknoten. Jenaische Zeitschrift für Naturwissenschaft, Bd. 50, S. 359–409.

(7) George, W. C. 1926. The histology of the blood of Perophora viridis (Ascidian). Jour. Morph. and Physiol., vol. 41, pp. 311–329.

(8) ———. 1930. The histology of the blood of some Bermuda Ascidians. Jour. Morph. and Physiol., vol. 49, pp. 385–413.

(9) Goodrich, E. S. 1898. On the nephridia of Polychaeta. Part II. Glycera and Goniada. Quart. Jour. Micro. Sci., vol. 43.

(10) Goss, C. M. 1928. Experimental removal of the blood island of Amblystoma punctatum embryos. Jour. Exp. Zool., vol. 52, pp. 45–64.

(11) Jordan, H. E. 1924. The significance of the spleen in the light of embryological evolutionary and experimental data. Virginia Medical Monthly, vol. 51, pp. 537–544.

(12) ———. 1932. The histology of the blood and the blood forming tissues of the urodele, Proteus anguineus. Am. Jour. Anat., vol. 50, pp. 215–251.

(13) Jordan, H. E., and Baker, J. P. 1927. The character of the wall of the smaller blood vessels in the bone-marrow of the frog, with special reference to the question of erythrocyte origin. Anat. Rec., vol. 35, pp. 161–183.

(14) Jordan, H. E., and Speidel, C. C. 1923. Studies on lymphocytes. I. Effect of splenectomy, experimental hemorrhage, and a hemolytic toxin in the frog. Am. Jour. Anat., vol. 32, pp. 135–187.

(15) ———. 1924. Studies on lymphocytes. II. The origin, function, and fate of the lymphocyte in fishes. Jour. Morph., vol. 38, pp. 529–548.

(16) ———. 1924. Studies on lymphocytes. III. Granulocytopoiesis in the salamander, with special reference to the monophyletic theory of blood-cell origin. Am. Jour. Anat., vol. 33, pp. 485–505.

(17) ———. 1925. Studies on lymphocytes. IV. Further observations upon the hemopoietic effect of splenectomy in frogs. Jour. Morph. and Physiol., vol. 40, pp. 461–477.

(18) ———. 1928. The hemocytopoietic effect of splenectomy in the salamander. (Preliminary abstract.) Anat. Rec., vol. 39, pp. 50–51.

(19) ———. 1929. Blood-cell formation in the horned toad, Phrynosoma solare. Am. Jour. Anat., vol. 43, pp. 77–101.

(20) ———. 1929. The origin and proliferation of thrombocytes in splenectomized salamanders. Proc. Soc. Exp. Biol. and Med., vol. 27, pp. 67–68.

(21) ———. 1930. The hemocytopoietic effect of splenectomy in the salamander, Triturus viridescens. Am. Jour. Anat., vol. 46, no. 1, pp. 55–90.

(22) ———. 1930. Blood formation in cyclostomes. Am. Jour. Anat., vol. 46, pp. 355–391.

(23) ———. 1931. Blood formation in the African lung-fish, under conditions of prolonged estivation and recovery. Jour. Morph. and Physiol., vol. 51, pp. 319–371.

(24) Kindred, J. E. 1924. The cellular elements in the perivisceral fluid of echinoderms. Biol. Bull., vol. 44, pp. 228–251.

(25) ———. 1926. A study of the genetic relationships of the "Amebocytes with spherules" in Arbacia. Biol. Bull., vol. 50, pp. 147–154.

(26) ———. 1929. The leucocytes and leucocytopoietic organs of an oligochaete, Pheretima

indica (Horst). Jour. Morph. and Physiol., vol. 47, pp. 435–478.

(27) Kollmann, M. 1908. Recherches sur les Leucocytes et le Tissu lymphöide des Invertébrés. Paris.

(28) Patten, W. 1912. The Evolution of Vertebrates and Their Kin. P. Blakiston's Son and Co., Phila.

(29) Prenant, M. 1922. Recherches sur le Parenchyme des Plathelminthes. Essai d'Histologie Comparée. Paris.

(30) Redfield, A. C., and Florkin, M. 1931. The respiratory function of the blood of Urechis caupo. Biol. Bull., vol. 61, pp. 185–210.

(31) Romieu, M. 1923. Recherches histophysiologiques sur le Sang et sur le Corps cardiaque des Annélides polychètes. Paris.

(32) Slonimski, P. 1931. Recherches expérimentales sur la genèse du sang chez les Amphibians. Arch. de Biol., T. 62, pp. 415–477.

(33) Van der Heyde, H. E. 1922. Hemoglobin in Thyone briareus Lessuer. Biol. Bull., vol. 42, pp. 95–98.

PROBLEMS IN GROWTH CHEMISTRY

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TO THE biochemist, growth means the increase in cell substance, in organic or inorganic cell constituents produced by the organism from food. The capacity of a cell for these compounds is limited, however, and growth will come to an early end unless the cells have also the property to divide. Cell division as such is therefore of paramount importance in the chemistry of growth though we usually think of it more as a cytological problem.

Without the presence of a living cell, the "food compounds" will not change into cells, not even into cell substances. No means has as yet been found to substitute for the cell in this respect. In the following discussion, this capability of the cell to produce cell substances from food will be called "catalysis." No special assumption is made regarding the mechanism of growth catalysts. The expression is used only to differentiate the growth machinery from the building material.

Growth is essentially a chemical synthesis. Cell substances are produced from food which is chemically different from the cell constituents. Synthesis is quite evident with green plants, each of which produces hundreds of different organic compounds from CO_2 plus nitrates and water. But even with carnivorous animals, which eat protein, fat and bones in order to produce protein, fat and bones, a considerable amount of synthesis is accomplished. The architecture of the protein in the cat muscle is quite different from that of the beef muscle from which it may have been built. The food protein is decomposed into small fragments, the amino-acids, by the digestive process, and with these building stones the cat protein is built according to a different style. More convincing still may be the formation of chromosomes of one animal from meat of another animal. A white dog being fed nothing but meat from black dogs, will not turn black. Its chromosomes remain unaffected by the black chromosomes of the food.

This change of food into cell substance is, at least in part, a chemical synthesis, and therefore it requires energy. The necessary amount may not be large, in some cases, but some energy is required. In normally nourished cells, energy is available in liberal amounts. The green plants obtain it from the light, the animals get it from respiration, i.e., from the oxidation of food, and bacteria provide for it by fermentation, which is also a chemical change of the food.

In what form the energy is liberated, and how it is applied in synthesis, we do not know. We may speak of it in terms of calories, but we have no proof that it is produced in form of heat.

OXIDATION-REDUCTION POTENTIALS

A possible explanation presents itself by the conception of potentials as prerequisite for work to be done. A certain minimum pressure is necessary to start a steam engine. It is not the amount of steam, or the size of the boiler that counts. The pressure decides whether or not the engine will run.

The energy liberated in a cell must neces-

sarily establish potentials. One g. of glucose liberates 82 calories when fermented to lactic acid. At the moment when this change takes place, the energy will be limited to the 2 lactic acid molecules just created. This would mean that the lactic acid molecules have a temperature about 82° higher than the rest of the cell (or an energy content in some other form corresponding to this difference of temperature). At the very moment of the splitting of the molecule, the potential difference between the new molecules and the surrounding cell contents is very high. This potential difference is capable of doing work.

Aside from osmotic potentials, the only potential in a cell which we have been able to measure so far, is the oxidation-reduction potential. It indicates the intensity with which a cell can reduce. For example, a certain minimum potential is necessary to reduce methylene blue to the colorless leuco-compound. Most living cells can do that; their reduction potential is strong enough. Only very few bacteria have a potential strong enough to reduce sugar so that hydrogen is developed. The reduction potential in the cells can be tested by injecting indicators.

Whether the reduction potential is used for growth, for synthesis, we do not know. Synthesis is frequently a reduction process, but similar effects are no proof for similar causes.

The reduction potential is brought about by certain compounds which can be oxidized reversibly, and act as oxygen catalysts. Methylene blue is such a substance. It stimulates respiration greatly. To this group belong also the sulphydryl compounds, like cysteine and glutathione, which have been known during the last twenty years to have a decided influence upon cell oxidations.

The presence of any one of these compounds in a solution will give it a definite reduction potential. This does not allow us to predict how much can be reduced or how rapidly, but we can say whether a certain reduction is possible or impossible in this system. For example, in the complete absence of oxygen, methylene blue at pH 6 will be reduced if cysteine is added, but not if glutathione is added (see fig. 1) while at pH 4 and pH 8, both solutions will reduce the dye.

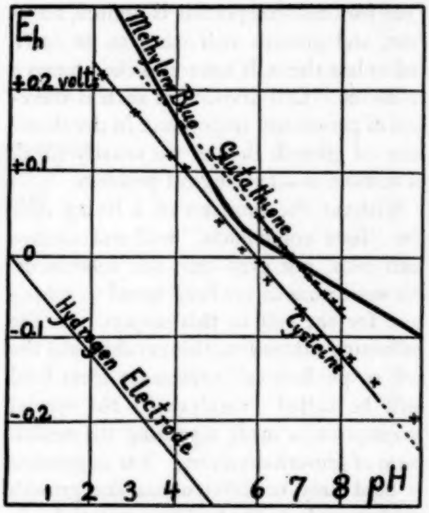


Fig. 1. The Reduction Potentials of Methylene Blue, Glutathione and Cysteine, at Different pH, Measured in Volts

SULPHYDRYL-COMPOUNDS

For about twenty years, the sulphydryl compounds have been known to be closely connected with the growth problem, as well as with the oxidations in the cell. Recently, Hammett, (1929) has shown them to be even more essential than had been believed before.

He observed that sulphydryl compounds are present in the largest concentration in those tissues where mitosis is most rapid, and within the cell, they are concentrated

in the nucleus. Lead salts which combine with the sulfur of the sulphydryl will prevent mitosis, but do not interfere with an increase of the size of cells. Very dilute solutions of various sulphydryl compounds, containing a few milligrams per liter, will cause a distinctly increased growth rate of plant roots or of paramecium. Quite interesting is the proof that the sulphydryl compounds have nothing to do with the increase in the size of the cell; they stimulate only cell division. Table 1, which is a compilation of parts of two extensive tables by Hammett, shows that sulphydryl compounds increase distinctly the frequency of mitosis, from 12.9 to 17.3 and from 14.7 to 21.5 per cent of all nuclei counted. At the same time, the cells were not enlarged. On the contrary, while the width remained unchanged, the length was shortened by the sulphydryl compounds. There is then a distinct "mitogenetic" effect brought about by the sulphydryl compounds. Ergothioneine, glutathione, insulin and di-thioglycollic acid were also found to give similar results.

The distinction between stimulation of nuclear division on one side and of general assimilative properties, i.e., chemical synthesis and increase in cell size and cell substance on the other side is important.

TABLE 1

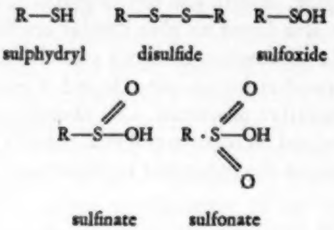
Influence of Thioglycollic Acid and of Cysteine on the Root Growth of Corn (Zea Mays)

Nuclear Counts, Each from 8 Roots						Cell Dimensions			
Total Nuclei		Dividing Nuclei		Percentage of Dividing Nuclei		Average Width of cells in μ		Average Length of cells in μ	
Control	Test	Control	Test	Control	Test	Control	Test	Control	Test
Thioglycollic Acid									
8,014	6,435	756	703	9.4	11.0	14.5	14.2	14.9	14.1
11,274	10,294	1,521	1,790	13.5	17.4	13.7	14.3	14.9	14.1
10,000	8,907	1,523	1,927	15.2	21.6	13.8	14.2	14.8	14.1
11,405	11,540	1,457	2,209	12.8	19.1	14.4	13.8	15.4	13.4
12,332	11,468	1,793	1,947	14.5	17.0	14.9	15.1	15.1	13.9
11,519	11,625	1,342	2,057	11.7	17.7	13.8	13.1	15.2	14.0
Average................................				12.9%	17.3%	14.2μ	14.1μ	15.1μ	13.9μ
Cysteine									
11,946	10,540	1,756	2,560	14.7	24.3	13.9	14.3	14.3	13.2
10,358	10,608	1,419	2,450	13.7	23.1	14.4	13.4	15.0	14.1
10,007	10,719	1,377	2,125	13.8	19.8	13.8	14.8	15.5	13.9
13,776	12,383	2,256	2,325	16.4	18.8	14.2	13.6	14.7	14.3
Average................................				14.7%	21.5%	14.1μ	14.0μ	14.9μ	13.9μ

Hammett found the sulphydryl compounds to stimulate cell division in all organisms which he tested; this included some infusoria, (paramecium and ameba), the regeneration of a cut-off foot of the hermit crab, (fig. 2), and the skin of mice.

The partly oxidized sulphydryl compounds, such as sulfoxides and sulfinates, retard growth. Hammett believes that cell division in organisms is regulated by a naturally occurring equilibrium be-

tween sulphydryl compounds and their various oxidation products. The oxidation stages are the following:



Addition of sulphydryl will disturb this equilibrium and produce faster cell division. Addition of partly oxidized sulphydryl will retard cell division.

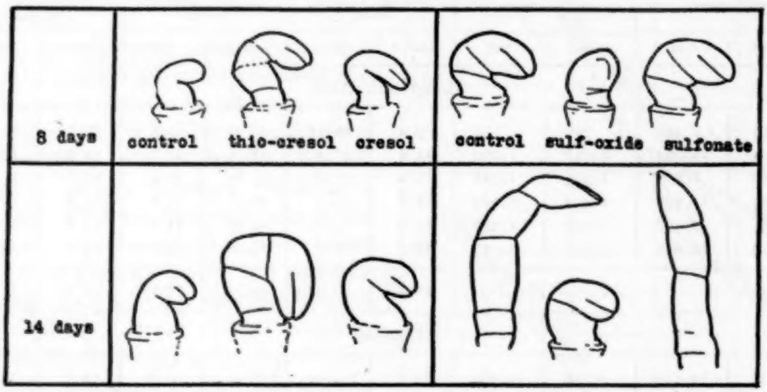


Fig. 2. Regeneration of the First Right Foot of the Hermit Crab (Pagarus longicarpus) in Solutions of Sulphydryl Compounds and Their Oxidation Products

This is the experimental evidence. Whether the oxidation-reduction potential of the cell will influence this equilibrium, we do not know. It seems probable, but the proof is lacking.

BIOS

In 1901, Wildiers made the observation that in a medium consisting of nothing but mineral salts, sugar, and ammonium salt, yeast will grow only if a large inoculum is used. Small quantities of yeast do not grow (Table 2). If a sufficient number of dead yeast cells is added, growth takes place (Table 3). He concluded that besides sugar, ammonia and minerals, the yeast needed a very small amount of an organic nitrogenous compound for which he suggested the name "bios." He added: "May this word soon be replaced by a chemical term." Today, thirty years later, we are just beginning to replace in part the word "bios."

A surprisingly large amount of work has been done on this problem which is entirely a bacteriological problem. Tanner, in his review (1925) lists 144 papers on bios, and the number has increased considerably since.

The great confusion, and the many contradictory results obtained by various authors are partly due to different definitions of the term bios. Some authors define it as a compound necessary for growth; there can be no growth without this compound as there is no growth without Ca or K. Others define it as being necessary for "healthy" or "normal" growth, allowing that a poor and slow growth is possible without this compound.

Robertson (1924) found that in a mineral ammonia sugar solution, yeast will grow in the first transfer, and in the successive transfers too, but the growth becomes weaker and weaker, and after about fifteen transfers, ceases altogether. Fulmer and Nelson (1923), however, could keep yeast growing through an unlimited number of transfers in a similar synthetic medium. There are various explanations: there is a great difference in yeasts, even in varieties of the same species. There may have been, in the minerals, lack of an tion of bios, on the cause of poor growth in sugar solution + NH_3 + minerals and of good growth when certain substances like meat extract, potato juice, orange or tomato juice, were added in small quantities. One of his associates, Lucas (1924) could separate the accessory food compound into two fractions each of which was inactive while together they increased the crop at least tenfold. One of the fractions has been identified by Eastcott (1928) as inositol $C_6H_{12}O_6$. The other fraction is still unknown.

TABLE 2

Wildiers' Bios. Growth of Yeast (measured by CO_2-Formation) in a Sugar-Mineral Solution + NH_3, with Increasing Amounts of Inoculum (g CO_2 from 125 cc. of culture)

	AMOUNT OF YEAST SUSPENSION ADDED			
	0.25 cc.	1 cc.	2.5 cc.	5 cc.
after 3 days	0	0	0.5	1.9
6	0	0.3	2.2	5.0
8	0.1	1.1	3.9	

TABLE 3

Growth of Yeast (measured by CO_2-formation) in a Sugar-Mineral Solution + NH_3 and + Increasing Amounts of Dead Yeast, from a Small Inoculum of 2 Drops of Suspension (g CO_2 from 125 cc. of culture)

	AMOUNT OF BOILED YEAST SUSPENSION ADDED				
	1 cc.	2 cc.	3 cc.	4 cc.	5 cc.
after 2 days	0	0	0.5	1.2	2.5
3	0	0	1.0	2.1	4.7
4	0	0	1.2	3.0	5.6

element necessary in very minute quantities. It must be remembered that Hopkins (1930) found that the alga *Chlorella*, for fair growth, requires 0.2 mg. of manganese per liter of solution. This amount was present in several of the c.p. chemicals on the market. If Robertson happened to have chemicals not containing the extremely small amount of some needed element, while Fulmer's chemicals contained it, the different results might be explained.

Miller worked on the other interpreta-

Buston and Pramanik (1931) working with the fungus *Nematospora gossypii*, found similar conditions in its growth, and with them, too, one of the fractions contained inositol as the active substance. Reader (1929) working with *Streptothrix corallinus* observed no effects with inositol while mannitol gave much larger crops. The concentration used, 0.5 per cent, is s large, however, that the possibility of the mannitol being used merely as source of energy is not entirely excluded. Since

yeasts and fungi are more closely related to each other than to *Streptothrix*, such a difference in response to different compounds is not surprising.

Some authors consider the absence of growth with very small inocula, as shown in tables 2 and 3, to be the real Bios problem. This may be just a case of extreme lag phase.

The lag phase is known to every bacteriologist. It is the period during which old cells transferred to a fresh medium adjust themselves to the new environment. When a culture of yeast or bacteria is transplanted, the cells do not multiply at once. It takes several hours, sometimes even days before the fastest growth rate possible in that medium is reached. During this lag period, the cells change morphologically as well as physiologically. Young, rapidly growing cells, when transferred, show no lag period.

There is one peculiar observation which appears at first to be contrary to expectations. The period of lag increases as the number of transferred cells becomes smaller. This has been observed by a number of bacteriologists, and the best example is probably that by Henrici (1929). He transferred from a yeast suspension decimal dilutions into flasks with sugar-peptone solution, and counted the cells per c.c. in the different cultures at short intervals. Table 4 shows the generation times, i.e., the time required by the yeast cell to double for each interval.

The lag period is the time which elapses before the fastest growth, or the shortest generation time, is reached. If the logarithms of the lag periods are plotted against the decimal dilutions, a good straight line is obtained, from which the lag periods for lower dilutions can be extrapolated, as shown in Table 5. It would take between 4 and 12 days before 2 cells per c.c. would show active growth. This suggests a parallel with the observations by Wildiers (Tables 1 and 2), especially when we consider that Wildiers' medium was less favorable than Henrici's.

TABLE 4

Influence of the size of inoculum upon the duration of the lag period of yeast in a sugar-peptone solution

	SIZE OF INOCULUM IN CELLS PER CC.				
	20,949,750	2,094,975	209,498	20,950	2,095
	Generation Time in Hours				
hours					
0–2	10.8	23.2	23.4		
2–4	3.0	4.1	>5.8		
4–6	3.1	1.4		42.1	
6–8	2.4	1.6	1.3		13.4
8–10	6.9	3.1	1.1		
10–12	6.2	2.5	1.2	2.7	
12–16	35.5	5.4	2.1	1.5	
16–20	301.2	10.6	4.0	1.1	20.3
20–24	105.5	46.8	9.2	1.5	15.3
24–36	188.5	58.3	75.3	4.6	2.2
36–48	668.8	98.8	101.7	50.8	6.3
48–72	>713.0	303.5	163.7	97.9	3.7
72–96		357.5	199.0	517.7	27.9
96–144	2256.0	612.5	1460.0	535.0	2833.3

It does not really matter whether this is what Wildiers meant by Bios. It is one of the growth problems to be solved. Wildiers had observed two handicaps of growth in synthetic media: the failure to grow with small inocula, and a poor yeast crop when no organic food besides sugar was offered. These two phenomena appeared to him as two symptoms of the same cause.

In this he was probably wrong. Lindner (1919) explained the Bios problem, which to him was the lack of growth of small inocula, as an oxygen problem. Yeasts have a tendency to undergo fatty degeneration with oxygen, and thus lose the ability to multiply. In the absence of oxygen, the yeast retains its power to grow in a fresh medium. Several other observations (compiled by Rahn, 1932, p. 202) point in the same direction. This suggests again a connection with the oxidation-reduction potential.

Most organisms have the power to oxidize their food. (The only exceptions are the anaerobic bacteria.) If there is no food, the cells will oxidize their own cell substance. Starving bacteria take up oxygen quite readily, and at a constant rate, (except again the anaerobic bacteria, Callow, 1924). This oxidation of cell substance means injury to the cells.

When the cells are normally nourished, they protect themselves against oxygen by the reduction potential; thus, they can counteract all damage by oxidation. In dry bacteria, lack of moisture inhibits liberation of energy for a potential, and the cells cannot prevent their oxidation. The rate of their death is proportional to the square root of the oxygen concentration (Paul, Birstein and Reuss, 1910).

Single isolated cells transferred to a new medium may have difficulty in establishing a reduction potential against the intruding oxygen, when they are old, and not ready to start operations at once. With a large seeding, the oxygen dissolved in the new medium is divided between many cells, and cells close to each other will have a better chance to establish normal working conditions. After a certain time, the medium itself will have a reduction potential which will relieve even the weakest cells from their paralysis by the oxygen.

TABLE 5

The lag period in Table 4 is passed

Observed:		
with an inoculum of	20,949,750 cells in	2–8 hours
with an inoculum of	2,094,975 cells in	4–8 hours
with an inoculum of	209,498 cells in	6–12 hours
with an inoculum of	20,950 cells in	12–24 hours
with an inoculum of	2,095 cells in	24–36 hours
Extrapolated:		
with an inoculum of	209 cells in	2–3 days
with an inoculum of	21 cells in	2.5–6 days
with an inoculum of	2 cells in	4–12 days

The relation between lag and reduction potential is supported by the observation that cysteine enables anaerobes to grow without protection against oxygen. Cysteine is known to establish a reduction potential (see fig. 1).

VITAMINS

Wildiers made his observations before vitamins had been discovered. It was only natural that afterwards, a good num-

ber of investigators thought that bios must be identical with vitamins. To this analogy dates back the attempt to measure the vitamin B content of foods by their effect upon yeast growth. It was ultimately found that though yeasts benefit greatly by products rich in vitamin, no quantitative parallelism could be established.

We now believe that most bacteria and yeasts can produce their own vitamins. While thus, the vitamin problem does not exist for the bacteriologist, nor for the botanist, it is a very vital one for the animal physiologist. He still searches for a final answer to the question why vitamins are necessary, and how they can act in the extremely minute quantities in which they are efficient.

The vitamin problem is the one of the growth problems with which all biologists are familiar. It needs only to be stated that they are essential for animal life, especially for growth, but also for repair, because the grown animal may also suffer from avitaminoses.

Two vitamins B and D have recently been obtained as pure substances, chemically well defined, and were found to be relatively simple substances, if compared with the molecule of enzymes, the smallest of which is thirty times that of the vitamin. Vitamin A is also known to have a molecular weight of only about 300.

HORMONES

The hormones are secretions of the glands of animals. Their presence or absence determines the normal and abnormal functioning of various parts of the body. The tasks of the hormones are quite specialized, and do not really belong to the general growth problem. They are, as far as they are known, relatively simple compounds.

Some twenty years ago, the German botanist Haberland found a hormone in plants. Wounds in plants would not heal easily if they were washed thoroughly, but if crushed plant cells were put on the wound, it would heal promptly. The healing factor was not destroyed by heat and Haberland, therefore, called it a hormone. Healing in most cases means a multiplication of cells, i.e., growth of cells which had already gone into a resting stage. The wound hormone is therefore a growth activator inducing the division of cells which would not do this without

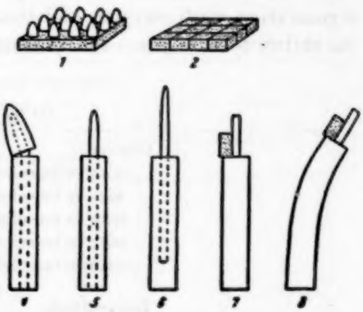


FIG. 3. METHOD OF OBTAINING AND DOSING THE "AUXIN"

1) agar block with 12 tips of coleoptiles; 2) same, after removal of tips, cut in cubes; 3) coleoptile with incision; 4) and 5) decapitation of coleoptile; 6) the first leaf is partly pulled out; 7) after decapitation of first leaf, the agar block is placed on the coleoptile; 8) one-sided growth and bending through one-sided growth stimulation.

the catalyst. The hormone causes a "mitogenetic," i.e., a mitosis-producing effect.

At about the same time, Boysen-Jensen observed a compound inducing growth of the tips of young plants; much later, some Dutch botanists realized the importance of this observation for the general growth problem (Went, 1931). The technique involved is relatively simple, and has become entirely standardized for quantitative work (see fig. 3). The coleoptile of an oat seedling is decapitated, the inner

leaf is partly pulled out, and also decapitated. This stops growth almost completely. If the tip is put back, the coleoptile starts to grow again. The compound causing growth will diffuse into agar, and if the agar is then put on top of the de-

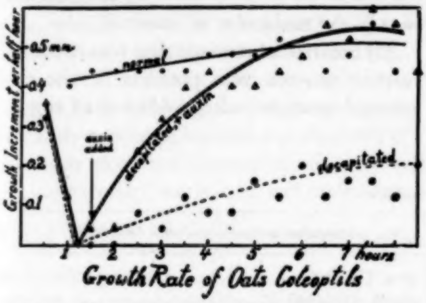


FIG. 4. GROWTH RATES OF COLEOPTILES, NORMAL, DECAPITATED, AND DECAPITATED WITH ADDITION OF AUXIN

capitated coleoptile, it will grow again. If it is placed on one side of the stump, only this side will grow and cause a bending. The angle is used as a measure of the quantity of the growth compound.

TABLE 6

Occurrence of Auxin, the Growth Compound of Coleoptiles, in Nature measured in Avena-Units

	AVENA UNITS
Diffusion product from corn seedling tips	about 300
Rhizopus reflexus	40–110
Bakers yeast	30– 40
Bacterium coli	about 50
Human feces	5–10
Human urine	about 400

This compound is a non-specific growth accelerator; it affects corn and oats as well as English daisies, and is found commonly in nature, as may be seen from Table 6.

The compound which the Dutch botanists call "auxin" has a molecular weight of about 350. It contains no P, N, or S, and is an acid soluble in ether (Kögle and Smit, 1931).

While it is claimed that there is no plant growth without this growth substance, it has not seemed so certain that it causes cell divisions. It seems that the main task of this compound is to cause a stretching of the cells.

THE RÔLE OF THE VARIOUS GROWTH COMPOUNDS

A number of compounds have been mentioned which are essential either for cell division, or for the increase in organic cell substance, i.e., for synthesis, or for growth generally. All these compounds, as far as they are chemically known, are relatively simple compounds, substances of the order of magnitude of sugar molecules (Table 7). This is surprising, for the catalysts of organic destructive processes, the enzymes, have a molecular weight of the order 10,000; they are nearly as large as protein molecules.

Frequently, the vitamins, hormones and similar compounds have been considered to be catalytic agents in the growth process. The small size of the molecule would not necessarily contradict their catalytic nature, but it opens new perspectives; it makes it appear possible that all these compounds may be only building stones for cell construction. Food serves largely as source of energy, and only a small part of it is used as building stones, as e.g., the amino acids.

Very small quantities of certain food substances, a fraction of a milligram of vitamin per person, or 1.7 mg. inositol per liter of medium, for yeast growth, or 0.2 mg. of manganese per liter of medium for algae, decide between life and death. It seems possible, that of certain special molecules in the cell, only very small quantities are needed for construction. The cell contains the nucleus with the

chromosomes which again contain the genes. Each gene is believed to be the carrier, or catalyst, for a certain cell property; consequently, each gene must be chemically different from all other genes. A gene is a very small unit, probably not larger than a very large protein molecule with a molecular weight of about 5,000,000 and a diameter of 24 mμ. Certainly, it is smaller than 100 mμ, for it is below the limit of microscopic visibility. If a special compound, e.g., inositol, should be needed to build one certain gene, it will require only one or a few molecules per cell to accomplish this. The question arises: Are there enough molecules in the extremely small amount needed to provide all cells with sufficient molecules?

This question can be answered, since the weight of molecules is known. For example, with inositol, one gram contains $\frac{6.06 \cdot 10^{23}}{180}$ molecules, because the molecular weight of inositol is 180. According to Eastcott (1928), 0.0167 mg. of inositol will permit the growth of 325,000,000 yeast cells.

0.0167 mg. inositol = $5.62 \cdot 10^{16}$ molecules. This leaves for each cell $\frac{5.62 \cdot 10^{16}}{325{,}000{,}000}$ = $1.7 \cdot 10^{8}$ molecules of inositol.

All inositol of the solution was used; no further growth was possible in the exhausted medium, after addition of sugar. The inositol had not been used for respiration; it could be obtained again quantitatively by boiling the yeast crop with HCl.

TABLE 7

Molecular weights

NITROGEN-FREE COMPOUNDS FROM ORGANISMS		NITROGENOUS COMPOUNDS FROM ORGANISMS	
acetic acid, $C_2H_4O_2$	60	urea, CH_4ON_2	60
oxalic acid, $C_2H_2O_4$	90	glycin, $C_2H_5O_2N$	72
lactic acid, $C_3H_6O_3$	90	leucin, $C_6H_{13}O_2N$	131
tartaric acid, $C_4H_6O_6$	150	tyrosin, $C_9H_{11}O_3N$	157
glucose, $C_6H_{12}O_6$	180	cystein, $C_3H_6O_2NS$	106
sucrose, lactose, maltose, $C_{12}H_{22}O_{11}$	342	glutathione	243
fat (tri-stearin) $C_{57}H_{110}O_6$	890	egg albumin	34,500
HORMONES		hemoglobin	68,000
adrenalin, $C_9H_{13}O_3N$	183	serum globulin	103,000
thyroxin, $C_{15}H_{11}ONI_4$	729	legumin	208,000
bios II (inositol)	180	hemocyanin (*Limulus*)	1,760,000
auxin of coleoptiles	330–352	hemocyanin (*Helix*)	5,005,000
VITAMINS		ENZYMES	
vitamin A	about 300	pepsin	39,000
vitamin B_1 (Windaus, Tschesche *et al.*)	251	rennet	11,200
vitamin D_1 and D_2 (Windaus, Luttringhaus *et al.*)	382	invertase	19,600
		emulsin	37,700

As another example, the relation of vitamins to the human body may be computed. Vitamins A, B, and C have a molecular weight of 251 to 382. The average of 300 will be used for this calculation. One g. of vitamin consists of $\frac{6.06 \cdot 10^{23}}{300}$ molecules; that makes $2.02 \cdot 10^{18}$ molecules per mg. The number of cells in

the human body can be estimated only to the order of magnitude. It is essential that the estimate be not too small, and it seems safe to assume that the average body cell is not larger than the red blood corpuscles. These may be considered as cylinders, 2μ high, and with a diameter of 7.5μ, which results in a volume of $88.5\mu^3 = 88.5 \cdot 10^{-12}$ cm.^{3}, or about $90 \cdot 10^{-12}$ g. This would amount to $800 \cdot 10^{12}$ cells for a human body of 75 kg, and this estimate is certainly too large because a good share of the body does not consist of cells. One mg. of vitamin, with $2.02 \cdot 10^{18}$ molecules, would allow $\frac{2.02 \times 10^{18}}{800 \times 10^{12}}$ = about 2,400 molecules per cell.

With yeast, practically all the cells had grown during the experiment with inositol. With vitamins, only the *new* cells would need the construction material, and also those which have to replace deteriorated cell substance. This latter amount can be estimated from the nitrogen loss during inanition to be not more than 1 per cent of the total weight daily. To provide each deteriorating cell of a grown person with one molecule of vitamin, 4×10^{-6} mg. would be needed daily.

While with inositol, there can be little doubt that it is a building stone for the yeast cell, there is no such proof with vitamins. It is a possibility, but it is also imaginable that the vitamins act really as catalysts, and not as building stones.

The same computation can be carried out for the various sulphydryl compounds. However, the situation seems to be different because we are not dealing with increase in cell substance, but only with the mitogenetic effect.

The growth compound of the coleoptiles probably belongs in the same group as the vitamins and the inositol. It is interesting to realize that only the tips of the coleoptiles can produce this substance while the rest of the plant appears to be unable to do so.

Whether hormones, generally, are just building material for the cell, seems rather doubtful, because in many instances, their function is not connected with cell division or increase in cell substance. It is imaginable that a new building material thrown into the blood stream, may be used to change the composition of certain groups of cells and thus make them function differently. But there is no experimental basis for such assumption. It is also imaginable that some hormones are building material while others act catalytically.

MITOGENETIC RADIATION

An entirely different viewpoint on the growth problem was offered by Gurwitsch, a Russian histologist who came to the theoretical conclusion that cell division must be excited by radiation. He proved this in 1923 by letting the radiation from one onion root fall on another onion root. The number of dividing nuclei in the exposed part of the root was much larger than on the opposite side.

The radiation goes through quartz, and thin cellophane, but not through glass nor gelatin, and belongs to the short ultraviolet, of about 2000 Å wave length. The same effect can be produced by the corresponding wave lengths of artificial light.

The original cumbersome method of counting the dividing nuclei in onion roots has since 1928 (Baron) been replaced by counting the percentage of buds on yeast. Yeast is spread over the surface of an agar block, and is then exposed to the biological radiation while a similar block is held under the same conditions, but unexposed, as control. After a definite time, the buds on the yeast cells are counted. This method does not appeal to the bacteriologist, because the percentage of budding

cells is no accurate measure of the growth rate, but it is entirely sufficient to prove whether or not the growth rate has been accelerated by radiation. The radiation is extremely weak. The photographic plate and the ordinary photo-electric cells do not register this radiation. The only physical instrument sufficiently sensitive for this radiation is the Geiger-Mueller counter modified for these wave lengths (Rajewsky, 1931).

It has been shown by Siebert (1928) and by Magrou (1931) that chemical processes may produce the same kind of radiation: the oxidation of glucose with permanganate or peroxide, the oxidation of pyrogallic acid, and the peptic digestion of protein.

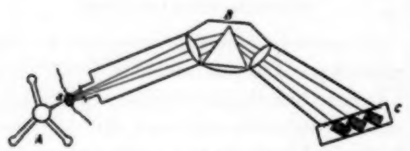


Fig. 5. Technique of Measuring Biological Spectra

A: Stand holding a frog sartorius, (*a*), excited electrically. *B:* quartz prism and quartz lenses of the spectrograph. *C:* glass plate, graduated according to wave lengths; on this glass plate are placed the agar blocks with the yeast.

In Gurwitsch's latest book (1932), the spectral analysis of various biological radiations is given. The radiation is sent through a quartz prism, and the spectrum is analyzed by a series of agar blocks with yeast, in place of the photographic plate (fig. 5).

It has been found that all oxidation processes give the same spectrum, and all proteolytic processes give another characteristic spectrum. The best studied spectrum is that of "glycolysis," i.e., the anaerobic decomposition of sugar. The spectra of glycolysis in blood, of alcoholic and lactic fermentation gave identical lines (fig. 6). The spectrum of the excited muscle does not check with any of these three spectra, but has some other lines besides. All of these spectra or radiations stimulate the growth rate of yeast.

If cells can radiate, and can also be affected by such radiation, then microorganisms in a solution must influence each other. This so-called "muto-radiation" has been studied by Baron (1930) with yeast. He found that with many cells in a drop of good nutrient medium, the percentage of budding cells is larger than with a smaller number of cells. In the latter case, they are too far apart, and the radiation from each cell is largely absorbed before reaching the other cells (Table 8).

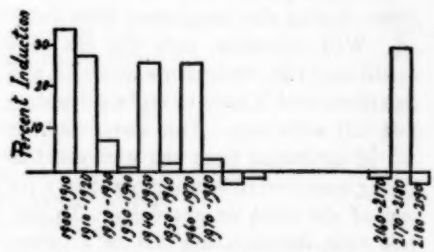


Fig. 6. The Spectrum of Glycolytic Radiation

To prove his point more clearly, Baron added gelatin to the medium. Gelatin absorbs these short wave lengths completely. The result was that even with large numbers per drop, the growth rate was not stimulated; it was the same as with a smaller inoculum (Table 9). All radiation was absorbed before it could reach other cells.

The explanation for extreme lag with very small seedings, as in the cases mentioned in Tables 2 and 3, is very simple. If Gurwitsch's theory is correct that a stimulus of ultra-violet light is needed to induce mitosis, a single cell in a medium can divide only if such radiation comes from outside.

This relation between the amount of inoculum and the length of lag has been explained above by the reduction potential. This suggests the question whether there is a relation between mitogenetic radiation and reduction potential. This does not seem very probable. The energy from cell radiation could hardly be of any account in the energy balance of a yeast cell which decomposes about 50,000,000 molecules of sugar per second (Rahn, 1932, p. 259). But it might be that it is the *form* of energy that counts, and that this special radiation might act like the spark in the powder barrel. The cell may be an amplifier for just this wave length.

Haberland, who discovered the wound hormone in plants, tested whether mitogenetic radiation would heal wounds. No effect was found at all while the contents of crushed cells caused normal healing. Gurwitsch stated thereupon that the chemical compounds were necessary for healing, but that they alone would produce no mitoses unless there was mitogenetic radiation at the same time. This is possible, but it can hardly be proved since all pulp from crushed plants radiates.

TABLE 8

Growth Acceleration by Mutual Irradiation with Saccharomyces ellipsoideus

INOCULUM	NUMBER OF BUDS PER 100 CELLS			
	Experiment No. 1		Experiment No. 2	
	8,000 cells	80,000 cells	8,000 cells	80,000 cells
start	0	0	0	0
after 3 hours	0	0	0	0
after 5 hours	3	16		
after 6 hours			5	49
after 7 hours	14	60		
after 10 hours			17	91
after 12 hours			35	91

TABLE 9

Prevention of Growth Acceleration by Absorbing the Mitogenetic Rays by means of Gelatin

INOCULUM	NUMBER OF BUDS PER 100 CELLS			
	Experiment A		Experiment B	
	8,000 cells	80,000 cells	8,000 cells	80,000 cells
start	1	0	0	0
after 3 hours	2	2	0	0
after 5 hours	18	21	12	15
after 7 hours	30	32		
after 8 hours			35	33
after 10 hours	41	42	48	52
after 12 hours			62	61

CONCLUSIONS

These are the outstanding attempts to understand the chemistry of growth. If

we could correlate all of them and explain one by the other, we could probably discover that there are many other factors still involved. But we cannot even correlate all the facts just mentioned.

Nevertheless, we can speculate about their interrelations, and some of these appear rather simple, though they may not be true.

It has been recently shown by the London biochemical school that vitamins A and B radiate, sufficiently to blacken the photographic plate in 3 days. This is suggestive, but we are far from having proved that vitamins act through their radiations.

The sulphydryl compounds, which are important for growth and which, according to Hammett, regulate the growth rate, have also a great effect upon the reduction potential. But there is no proof that this potential is essential for growth.

The bios of the bacteriologist may be nothing but the establishment of a reduction potential, and may thus link with Hammett's sulphydryl compounds. Some other facts about bios can be best accounted for by mutual irradiation of microörganisms. However, certain experimental facts prove also the need of definite chemical compounds in minute quantities for cell construction.

The auxin of the Dutch botanists stands a little outside of the discussion. It does not seem to be the cause of cell multiplication. It brings about the stretching of the cells, and is therefore necessary for growth; besides it, however, there must be still the "mitogenetic" effect, either chemical or physical.

The necessity of ultra-violet radiation for cell mitosis cannot be considered as proved. All proof so far has shown only the stimulation of the growth rate by such radiation. Unquestionably, the physical effect can be only part of the growth process since the most outstanding indication of growth is chemical synthesis which requires chemical reactions.

Rather surprising is the observation that the outstanding chemical substances in cell synthesis are relatively simple compounds while the agents of digestion and energy supply are from 10 to 100 times as large. The enzymes are of the order of magnitude of simple protein molecules while the hormones, vitamins, sulphydryl compounds, bios and auxin, have a molecular weight similar to that of sugar.

This simplicity suggests that at least some of these compounds may be nothing but building stones for the cells which are needed in very small quantity, but are nevertheless absolutely indispensable, and cannot be manufactured by the cell itself. It is also possible, however, that these compounds may act as catalysts to bring about necessary chemical reactions in the cell.

LIST OF LITERATURE

Baron, M. A. 1928. Centralblatt f. Bakteriologie, II. Abt., 73, 373

——. 1930. Planta, 10, 28

Boysen-Jensen. 1910. Berichte d. Deutschen Botan. Gesellschaft, 28, 118

Burton, H. W., and B. N. Pramanik. 1931. Biochem. Journal, 25, 1656

Callow, A. B. 1924. Biochem. Journal, 18, 507

Eastcott, E. V. 1928. J. Physical Chem., 32, 1094

Fulmer, E. I., and V. E. Nelson. 1923. J. Infect. Diseases, 33, 130

Gurwitsch, A. 1932. Die mitogenetische Strahlung, Berlin, Springer

Haberland, G. 1929. Biolog. Centralblatt, 49, 226

Hammett, F. S. 1929. Protoplasma, 7, 297

Henrici, A. T. 1928. Morphologic Variations and the Growth Rate of Bacteria. Springfield, Thomas

HOPKINS, E. F. 1930. American Journal of Botany, 17, 1047

KÖGL, F., AND A. J. HAAGEN SMIT. 1931. Koningl. Akad. van Wetenschappen Amsterdam, 34, 1411

LUCAS, G. H. W. 1924. J. Physical Chem., 28, 1180

MAGROU, J., AND M. MAGROU. 1931. Ann. des Sciences naturelles; Zoologie; 14, 149

PAUL, TH., BIRSTEIN AND REUSS. 1910. Biochem. Zeitschr., 25, 367

RAHN, OTTO. 1932. Physiology of Bacteria; Philadelphia, Blakiston

RAJEWSKY, W. B. 1931. Physikalische Zeitschr., 32, 121

READER, V. 1929. Biochem. Journal, 23, 61

ROBERTSON, R. C., 1923. Journal of Infect. Diseases, 32, 152

SIEBERT, W. W. 1928. Biochem. Zeitschr., 202, 105

TANNER, F. W. 1925. Chem. Reviews, 1, 397

WENT, F. A. F. C. 1931. In vol. II of Kostytschew und Went, Lehrbuch der Pflanzenphysiologie, Berlin, Springer, p. 282

WILDIERS, E. 1901. La Cellule, 18, 313

WINDAUS, A., LÜTTRINGHAUS, LINSERT AND WEIDLICH. 1932. Liebigs Annalen, 492, 226

WINDAUS, A, LÜTTRINGHAUS, AND DEPPE. 1931. Liebigs Annalen, 489, 252

WINDAUS, TSCHESCHE, RUHKOPF AND SCHULTZ. 1932. Zeitschr. f. physiologische Chemie, 204, 123

THE PROGRESSION FACTOR IN INSECT GROWTH

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THE general curve of growth has been often discussed in recent literature. The present paper will deal only with the discontinuous and abrupt growth of the Arthropoda, as demonstrated in insects. The historical development of the problem has been reviewed by Calvert and Bodenheimer.

The main result of these studies is the verification of Przibram's growth factor. Studying the growth of *Sphodromantis viridis*, he found a quotient of 2 for the weight of every stage as divided by the preceding one. For length, the same quotient proved to be 1.26 ($=\sqrt[3]{2}$). Adding some earlier data on Crustacea (by Brooks, and others) to these results, Przibram felt justified in stating these quotients to be a general rule in the growth of Arthropoda. Bodenheimer extended these studies to all insect orders. His researches showed that in very frequent cases between two moults, there might be two or more doublings of body weight. These non-manifested divisions had been called "latent divisions." Such latent divisions had been found in the growth of Orthoptera, Odonata, and Rhynchota. The Phasmid *Carausius morosus* (Eidmann) may serve as example (see Table 1).

The number of the latent divisions increases considerably in the holometabolic insects. The Tenthredinidid *Cimbex 4-maculata* (Bodenheimer) is here taken as an illustration (see Table 2).

A further increase of latent divisions between the actual moultings may obscure the progression factor. The weight of the Giallo Vittorio race of *Bombyx mori* increases as shown in Table 3.

But if we consider the whole series from the primitive cases like *Carausius* up to the most complicated like *Bombyx*, it will be readily understood that the latter are only deviations from Przibram's principle.

The average quotient for 92 series of quotients for the progression in growth of length was exactly 1.265. A similar series for the progression in weight-growth is represented in Table 4.

It will be seen that the average quotient for all these series is exactly 2.005. The deviations from 2 disappear, if we take the + and − signs into consideration. The table starts with cases like that of *Sphodromantis* and *Toxoptera*, in which each calculated division coincides with an actual moult. In *Carausius* and *Schistocerca* we find one latent division in each. These interpositions have the result that the weights for one or two stages fall between these calculated values. But agreement between the other parts of the series and the calculated data could not be explained without Przibram's principle. The same is true for the more complicated cases.

An interesting discovery in the course of these researches was the fact that the females of nearly all Acrididae, Phasmidae, and probably also Mantidae, doubled their weight between the last moult and the beginning of the oviposition period. As the total weight of the mature ovaria is only one-third of this increase, we must regard the pre-oviposi-

tion period as an additional development stage, which is lacking in the males of these orders.

The agreement with Przibram's factor is obvious. Alpatov (1927) substantiated the same conclusion on *Drosophila*. But

TABLE 1

Observed body weight (in mgs.)	3.6		11	25	50	110	230	480	1,008
Calculated body weight	3.6	7.2	14.7	28.8	57.6	115.2	230.4	460.8	926.2
Observed body length (in mms.)	15.5	22.8		29.5	38.7	51.0	64.7	80.9	
Calculated body length	15.8	20.0	25.3	31.9	40.3	50.9	64.2	80.9	

TABLE 2

Observed body weight (in mgs.)	3.5	7.0	—	39	—	140	—	448	903
Calculated body weight	3.2	7.5	15	29	57	113	226	452	903
Observed body length (in mms.)	7.0	12.3		18.5	—		—	36.0	
Calculated body length	7.0	11.2	14.2	18.0	22.7		28.6	36.0	

TABLE 3

Observed (in mgs.)	0.52	—	—	—	7.4	—	43	—	—	200.1	—	977.6	—	4,100
Calculated	0.5	1	2	4	8	16	32	64	128	256	512	1,025	2,050	4,100

TABLE 4

SPECIES	NUMBER OF MOULTS	NUMBER OF DIVISIONS	ABSOLUTE GROWTH	AVERAGE QUOTIENT OF WEIGHT INCREASE
Sphodromantis viridis	9	9 (10?)	540 (1,080?)	2.03
Carausius morosus	6	7	278	1.98
Schistocerca gregaria	5	7	126	1.90
Dociostaurus maroccanus	5	7	77	1.76
Toxoptera graminum	4	4	16	2.01
Bombyx mori: Giallo Vittorio	4	13	7,884	2.23
Bombyx mori: Nipponoshiki, Gen. 1st.	4	13	8,417	2.11
Bombyx mori: Nipponoshiki, Gen. 2nd	4	12	3,615	1.87
Bombyx mori: Chan Toung	3	12	5,005	1.97
Philosamia ricini: India	4	10	1,091	2.03
Philosamia ricini: Palestine	4	12	4,843	1.98
Pieris brassicae	4	10	1,024	1.97
	5	10	782	2.11
Dytiscus marginalis	2	6	52	1.87
Epilachna chrysomelina	3	5–6	177	1.98
Apis mellifica	—	11	1,576	2.22
Cimbex 4-maculata	4	8	258	2.05
Average				2.005

Some additional material from recent publications may be discussed. The growth factor of some Odonata (Calvert) is as shown in Table 5.

nevertheless the principle has again and again been misunderstood. Two typical cases from recent publications may be quoted. Larson in studying the

TABLE 5

SPECIES	ACTUAL	CALCULATED	GROWTH QUOTIENT
Lestes viridis	9	12	1.227
Agrion pulchellum	9	9	1.263
Anax junius	13	15	1.253
Pantala flavescens (Honolulu)	10	13	1.272
Pantala flavescens (Philadelphia)	9	10	1.272
Sympetrum vicinum	10	10	1.247
Nannothemis bella	12	12	1.253
Average			1.263

TABLE 6

OBSERVED DATA	CALCULATED DATA	DEVIATION	QUOTIENT	REMARKS
Breadth of Head in mms.				
		per cent		
1.010	.958	+5.4		
1.346	1.207	—	1.33	
	1.521			One latent division
1.807	1.917	−5.6	1.34	
2.407	2.435	−1.1	1.33	
3.068	3.068	+0.0	1.27	
Breadth of Body in mms.				
1.238	1.247	−0.7		
	1.571		1.45	
1.793	1.979	—	1.42	
2.541	2.494	+1.9		Two latent divisions
	3.143	—	1.42	
3.616	3.961			
4.991	4.991	+0.0	1.38	

TABLE 7

AT 10°C.			AT 25°C.		
Observed	Calculated	Deviation	Observed	Calculated	Deviation
		per cent			*per cent*
2.3	1.8	—	2.3	2.1	+9.5
	3.5			4.2	
	6.9			8.4	
13.1	13.9	+5.8	16.5	16.8	−1.8
	27.9			33.6	
60.9	55.9	−10.0	87.2	67.2	
	111.7			134.4	
223.4	223.4	+0	268.8	268.8	+0

growth of *Notonecta glauca* concludes that his quotients do not agree with our conclusions. As a matter of fact, they do agree well enough (see Table 6). These data fully agree with earlier results (Bodenheimer) and confirm that in the linear growth of Heteroptera there are always one or two latent divisions.

For the Japanese Beetle (*Popillia japonica*), Ludwig denies the value of Przibram's principle. But his data mainly confirm it, if we consider that *Popillia* as a holometabolic insect with many divisions cannot show a full agreement. The body weight (in mgs.) after the different moultings is as shown in Table 7.

It would be unreasonable to expect to find that in every case of insect growth the quotients follow our rule. But the comparison of all analyses, which are present in the literature, allows one to draw the conclusion that insect growth in the more primitive conditions of Hemimetabola follows a progression factor of 2 or $n \cdot 2$ in the growth of weight and of $\sqrt[3]{2} = 1.26$ or $n \cdot 1.26$ in the growth of length. It is the increase of latent divisions which obscures these relations somewhat. But even here Przibram's principle is valid.

One misunderstanding, finally, must be removed, this having often been enunciated in literature on the subject. Przibram, Bodenheimer and others are believed to assume that each division is accompanied or even provoked by a contemporaneous division of all body cells. This may be the case and the recent statements of von Buddenbrock that insect moulting is induced by hormones may point in this direction. But no definite statement or special research in this respect has ever been made.

SUMMARY

Insect growth follows a progression factor of 2 or $n \cdot 2$ for weight, and of $\sqrt[3]{2} = 1.26$ or $n \cdot 1.26$ for length. The increase of latent divisions in the Holometabola obscures these relations, without invalidating them.

LIST OF LITERATURE

(1) Alpatov, W. W. Growth and variation of Drosophila larvae. *Journ. Exper. Zool.*, 52, 1929, pp. 407–437.

(2) Bodenheimer, F. S. Ueber Regelmässigkeiten im Wachstum der Insekten. I. Das Längenwachstum. *Deutsche Entom. Zeitschr.*, 1927, pp. 33–57.

(3) ——. Idem. II. Das Gewichtswachstum. *Archiv f. Entw. Mech. d. Organismen*, 126, 1932, pp. 554–574.

(4) Brooks, W. K. Report on the Stomatopoda collected by H. M. S. Challenger during the years 1873–1876. Challenger Reports, 16, 1886, Zool. pt. 45. 116 pp.

(5) Calvert, P. C. Different rates of growth among animals with special reference to the Odonata. *Proceed. Amer. Philos. Soc.*, 48, 1929, pp. 227–274.

(6) Dyar, G. H. The number of moults of lepidopterous larvae. *Psyche*, 5, 1890, pp. 420–422.

(7) Eidmann, H. Untersuchungen über Wachstum und Häutung der Insekten. *Zeitschr. Morph. Oekol. d. Tiere*, 2, 1924, pp. 567–610.

(8) Larsen, O. Biol. Beobachtungen an schwedischen Notonecta-arten. *Entom. Tidskrift.* 1930, pp. 219–247.

(9) Ludwig, D. The effect of temperature on the growth curves of the Japanese Beetle (*Popillia japonica*). *Physiol. Zool.*, 5, 1932, pp. 431–447.

(10) Przibram, H., and Megušar, F. Wachstumsmessungen an *Sphodromantis bioculata* Burm. I. Länge und Masse. *Arch. Entw. Mech. d. Organismen*, 34, 1912, pp. 680–741.

Further literature is quoted in (2), (3), (5), (9).

NEW BIOLOGICAL BOOKS

The aim of this department is to give the reader brief indications of the character, the content, and the value of new books in the various fields of biology. In addition there will frequently appear one longer critical review of a book of special significance. Authors and publishers of biological books should bear in mind that THE QUARTERLY REVIEW OF BIOLOGY *can notice in this department only such books as come to the office of the editor. The absence of a book, therefore, from the following and subsequent lists only means that we have not received it. All material for notice in this department should be addressed to Dr. Raymond Pearl, Editor of* THE QUARTERLY REVIEW OF BIOLOGY, *1901 East Madison Street, Baltimore, Maryland, U. S. A.*

AMERICA TODAY AND MAYBE TOMORROW

Being a review of *Recent Social Trends in the United States. Report of the President's Research Committee on Social Trends.* 2 vols. New York (McGraw-Hill Book Co.), 1933. Pp. xcv + 1568. $6\frac{3}{16} \times 9\frac{1}{4}$. $10.00.

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I

The presidency of Woodrow Wilson marked the turn of an era in American life in more ways than one. We have been regaled in recent years with a series of books about the pleasanter aspects of living in the "decades" immediately preceding the coming of Mr. Wilson and the World War. These treatises have made clear by sharp contrast the changes and innovations which have necessitated new adjustments and adaptations by the human organism. But one thing that developed in Mr. Wilson's administration, and for which he was in no small measure personally responsible, has either been overlooked entirely by social and political philosophers, or its significance has been somewhat less than adequately apprehended.

I refer to the beginning of the Era of the University Professor as an Important Person in Public Affairs. Up to the time of Mr. Wilson's ascent to the throne university professors were almost universally thought of, if at all, by Really Important People in the United States as "those —— damned professors." But by the middle of 1917 all that had been changed. Great men were being bossed by professors, and liking it. The professor had at long last come into his own in this great republic, and was not only having a grand time, but making it clear to everyone that he was by no means such a silly fool as he had been supposed to be. And he is not only still holding the place so gained but marching onward and upward on this same pathway. To be sure neither Mr. Harding nor Mr. Coolidge showed any particular comprehension of what academic people could do for them. But after all they, each in his own way, were so busily occupied with their personal affairs, again of a totally different kind in each case, that they quite pardonably could not be expected to take a broad view about the utility and importance of the professoriate. And also it must not be forgotten that Mr. Hoover was in the cabinets of both. From the very beginning of his career he has fully appreciated the value of scholarly learning, and drawn unstintingly upon the potentialities of its possessors to further his enterprises, both private and public. Doubtless some day a diligent seeker for the adornment of a Ph.D. will make a proper statistical analysis of the total personnel of the various commissions set up by and through Mr. Hoover alone since April 1917. When this is done the truth of what has been said above will be proven by a documentation overwhelming in its magnitude and appositeness.

The process still goes on. According to what we read in the papers Mr. Roosevelt

needs and heeds the advice of a professor about almost, if not quite, everything he does. Before his administration is six weeks old it may be confidently expected that his henchman, the redoubtable Louisiana Kingfish, will be taking his orders from a dean, or conceivably even a mere assistant professor.

All this is, in the highest degree, commendable from the point of view of the nation's affairs, and that viewpoint alone is our concern at the moment. In the long run we may expect to benefit as England, France, and Germany—indeed every European country I can think of except Russia and perhaps such small fry as Portugal—have benefited for generations by holding learned men in adequate esteem in human affairs generally. There is, of course, another and potentially sadder aspect of the matter. It remains still to be seen how the American professor will bear the spiritual prosperity which inheres in the burgeoning of His Era. The advancement of learning has been generally regarded as the primary business of the university professor. What will be the ultimate effect upon this really difficult and time consuming task of gaily barging into politics, theology, business, and front pages generally? The answer is not yet of record, but, as I have already said, this matter is not our present concern.

II

The processes of natural growth and development of professorial influence in public affairs which have been inadequately outlined above have now in the last days of the Hoover administration reached their highest point. In September, 1929, Mr. Hoover asked "a group of eminent scientists" to tell him whether a survey of social trends in the United States could be made. The answer was so immediate and reassuring that in December of the same year he was able to appoint a Committee consisting of five professors and one officer of a foundation to do the job. The chairman was Dr. Wesley C. Mitchell, easily the ablest and most distinguished American scholar in the so-called social sciences. Steam for the research was generated by a "grant of funds." The Committee of six called to their aid in the task, for one purpose or another, 20 "federal departments and bureaus;" over 100 "research bureaus and organizations," including Kiwanis International, Otis Elevator Company, Women's National Republican Club, and Zonta International, among others more conventionally identified with research enterprises; and so many individuals that merely to list their names and institutions required over 13 pages of close-set print. Of these individuals the vast majority belong in the upper levels of the college and university hierarchy. Here, as never before, the professoriate got a chance to come to grip *en masse* with the great realities of life in troubled times.

The results of this prodigious activity are now before us, having been released on the Monday following last New Year's day. That is to say 202.34 cubic inches (measured unbound) or just a pint short of two gallons, at least, of the results are now available, according to measurements and calculations laboriously made by Reginald the Office Boy. They are to be supplemented at leisure by 13 more volumes of monographs giving additional data to support and extend the conclusions reached in the Report itself. The two volumes of the Report contain a total of 1663 pages, divided into 29 chapters. Four of these chapters emanated from three members of the original Committee (two by Ogburn, and one each by Merriam and Odum). The remaining twenty-five chapters were written by rather more than the same number of persons of repute in the various fields discussed, drawn mainly from universities, and to a relatively much smaller extent from public and private research and welfare organizations of various sorts. In a few cases the men selected by the Committee for the tasks were literally and beyond argument or question the foremost living authorities in their respective fields. In some other cases they quite as clearly could by no stretch of the imagination be regarded as occupying any such position in the opinion of their professional colleagues. But after all somebody had to be chosen to do the work, and somebody had to do the choosing. It would have been a major miracle and something really to worry about if the six who

were responsible for the choosing had turned out to be wholly devoid of human and academic and scholarly prejudices and jealousies; or had been wholly unaware that they themselves were the appointees of a particular person of a certain station in life. Of the six members of the original Committee two are professors in the University of Chicago, one in Columbia University, one in the University of North Carolina, one in Harvard, and one not in academic life. Twenty of the 29 chapters of the report have as sole or part authors university or college men (not counting the persons designated as "with the assistance of "). There were 26 such authors (counting each individual every time he appears). In this list of authors the University of Chicago appears 9 times, Columbia 3 times, University of North Carolina 3 times, Harvard once (total to here 16). Yale contributed one chapter with two joint authors, and the remaining 8 authors each represent a different university or college.

These authors have produced a sound, workmanlike job. A tremendous mass of statistical and other data is digested and made handily available to students in these volumes. While in every chapter I have examined with care there are points made that are open to argument and about which competent students may disagree, there can be no doubt that this report will stand for some time as a useful reference work. A few of the chapters are masterpieces; notably those by O. E. Baker and Edgar Sydenstricker. A technical criticism that can be made of the report as a reference work is that the index is unworthy of the content. There is no author index at all, and no names appear in the subject index. Furthermore the subject index by no means conforms to the highest standards of modern scientific indexing.

III

What of the soul of *Recent Social Trends*, now that we have seen something of its anatomy and embryology? The answer is that it gives a wide-ranging and detailed picture of certain aspects of the United States as it is today, painstakingly painted in durable and quiet tones, calculated on the whole to soothe rather than excite the observer, and with touchy topics either omitted or treated as the Best People would wish them to be. According to the index "socialism" is mentioned on but one page out of 1663. There it is coupled with "fascism," "sovietism," and "trade unionism," and we are told that the American public has "remained relatively docile" in regard to such matters.

It seems improbable that anyone is ever going to get angry over these volumes, or alternatively to burst into paeans of praise about them to his neighbors. But after all the object of the enterprise was not to stimulate but first to describe and then perhaps guide, or prophesy, or both. As a description of the American scene as the Committee sees it today, the volumes are meticulously accurate. If one were to venture upon any general criticism of a work so well-intended and painstakingly wrought as this is, it would perhaps first include some regret at the nearly complete absence of comparative discussion and appraisal. After all, other countries and societies are older than ours and have accumulated a body of experience about their own ups and downs possibly useful in interpreting our own. Anatomists long ago learned that a description of the human body, however detailed and precise, yielded a much inferior understanding of its anatomy than was obtainable when its structures were compared with those of other animals. Indeed it is only in this way that any real insight into the meaning of human anatomy has come.

Another matter deserving of mention is the effect upon the end-product of the manner of its preparation. Apparently with the purpose of making the final report "sound" in the sense of containing nothing to which anyone could take exception, the several chapters—at least a great many if not all of them—were sent for criticism and suggestion to various people supposed in each case to know something about the subject under discussion. At first glance such a plan seems highly commendable. It appears to safeguard against anything like intellectual arrogance and such-like sins. But the method nevertheless has serious drawbacks. It obviously tends to reduce the whole performance to that dead-level of inoffen-

sive intellectual mediocrity which characterizes a departmental bluebook or census report. Anything like an original idea has small chance of survival in such a scheme. The matter is syllogistic, in this way: (1) Any new idea different from the prevailing mode of thought is presumed not "sound" because offensive to the opinions of "sound" authorities; (2) A chapter (and constructively a book) contains one or more new—that is, different—ideas; (3) Therefore that chapter (or book) is not "sound" in its present form and must be altered until it is. In short, above everything else, the manner of thinking and writing characteristic of such men as William Graham Sumner and Vilfredo Pareto (neither of whom, so far as I have been able to discover in the absence of a name index, is mentioned in these volumes) is to be avoided like a pestilence. The technique of a Calvin Coolidge is safer and "sounder."

It seems to me that the consequences of this mode of reasoning are evident in not a few of the chapters, though happily not in all.

IV

Just because it is chiefly a picture of our present day world *Recent Social Trends* inevitably and immediately calls into the reader's mind a comparison with another book, less than one-fourth as long, published some five years ago. I refer to *Les États Unis d'aujourd'hui* by André Siegfried. This was a book written for the purpose of describing the American scene realistically as it exists. It too indulged in a bit of modest prophecy. In short M. Siegfried and the President's Committee aimed at precisely the same target. There is not the smallest doubt that the former sunk his steel-jacketed bullets in the very center of the bullseye. Competent judges all over the world examined the target after he was through shooting and agreed with substantial unanimity about his score. In the literal and precise sense of the words *Les États Unis d'aujourd'hui* attracted world-wide attention and deeply influenced serious public opinion relative to the United States, in all countries of the world except the United States. It was translated into the languages of virtually all civilized peoples. Factually sound and thorough but never pedantic, it penetrated with an almost uncanny insight into the very bowels of American life, and lured the unwearied reader on to its ultimate page by the charm of its style, the vigor and sweep of its reasoning, and the readiness of its wit and good humor. This remarkable book was written by one professor (French) who received, to the best of my knowledge, no "generous grant of funds" whatever to spur him to the task.

As I have already pointed out, and must again emphasize, there is a remarkable parallelism, in respect of their aims, between *Recent Social Trends* and *Les États Unis d'aujourd'hui*. The marksmanship achieved by the two books is, however, singularly different.

Perhaps when M. Siegfried reads this report—as he surely will—he will be reminded of the plaintive remark of Dr. Johnson's old school-mate, who met him again many years later when the learned Doctor was under full head of pontifical steam. "Doctor," he is reported to have said, "I have often tried to become a philosopher, but cheerfulness will keep breaking in."

V

It has been mentioned above that besides its primary descriptive object the President's Committee felt constrained to prophesy or to be constructive when, as, and if the circumstances so moved them. It is upon this aspect of the effort that I wish next to focus attention. Not all of the authors appear to have experienced this urge. But a good many did. Direct quotation seems to be the most effective method here. Unfortunately such quotation must be brief, and consequently cannot do full justice in all cases to the several authors' arguments. Insofar as this is so I tender my apologies in advance. Some of the quotations gain in significance if read aloud slowly, and the implications of all should be pondered over.

Old John Smith, Taxpayer, will be cheered by the following prospects:

> The development of the new super-city points, therefore, to the need of some sort of super-metropolitan government. (p. 496.)
>
> A coherent and active policy as regards the con-

sumer does not exist throughout the government bureaus in Washington at the present time. Historically this has its roots in a long tradition of focusing attention upon the productive forces of the nation, of identifying consumer welfare with business prosperity, and of over-dependence upon the rational adequacy of the consumer's unaided choices. Whether something resembling a Department of the Consumer in Washington, coordinate in budget and power with the strongest of the present departments, is indicated is a secondary question. (p. 911.)

The state may be expected to increase rather than diminish its contributions [to the promotion of the arts] even in days of financial stringency. (p. 1007.)

More specifically, the work of governmental [health] agencies will probably grow, and these agencies, confronted with real needs for therapeutic treatment not being provided elsewhere, will probably give more attention to the function of treatment. (p. 1110.)

Also, the prospect is that the federal government will extend its criminal jurisdiction because of the increasing importance of the interstate aspects of many crimes. (p. 1166.)

The trend which is most important in marking the probable future developments in social welfare is the absorption of activities as a part of public administration in increasing numbers and at an accelerated rate. (p. 1222.)

Technically, the emerging needs appear to be: (1) a more adequate public relief, adapted in principle and methods to meet the demands of social change and emergency and economic cycles and depression; (2) the development of a plan for social insurance which will guarantee security and eliminate more and more the strain of social hazards and fear; and (3) social planning which will bring to bear the fullest utilization of social science and social research and their application through social work and public administration. (p. 1271.)

One factor which should operate to reduce the present burden of taxation is the decline in the general price level. In appraising the strength of this factor, however, it must be remembered that over 50 per cent of all taxes are expended for salaries, wages, and pensions. . . . . Approximately a quarter of the country's tax collections are expended for interest and redemption of indebtedness. (p. 1389.)

Those who believe that the government ought to help them in their efforts to curtail the pleasures of people of whom they do not approve will derive renewed hope and courage from the following:

Another problem of a different kind is the devising of ways and means of better governmental supervision and control of commercial amusements. This involves suitable measures of control over motion pictures and radio broadcasting, and the regulation of dance halls, pool and billiard rooms, cabarets and roadhouses, burlesque theatres, horse racing and other forms of amusement provided on the commercial basis. (p. 956.)

Subtle and profound thinking, and penetrating logic delight every intelligent man. Here is a morsel for his delectation:

Increased divorce is due to the weakening of the functions which served to hold the family together, and no doubt of public opinion, which would appear to be correlated with the exercise of these functions. If, say, six of these eight functions or bonds are weakened, then more divorce is to be expected, unless there is a corresponding strengthening of the other two. The future stability of the family will depend much more on the strength of the affectional bonds. (p. 708.)

Finally the *Social Trends* symphony, after developments, variations, recapitulations, and so on, returns at the end to the keynote. And how this will please everyone who admires the principles of liberty and the rights of man upon which the government of the United States was founded, and which were so carefully embodied in its Constitution by the founding fathers!

If all this seems speculative, we may turn to the development of governmental art in the period of the World War. Under the stress of a national emergency the government responded with surprising energy and efficiency. The subordination of private to public interest, the facility in recruitment of the necessary talent when the boycott on governmental service was lifted, the indifference to established precedent in administrative or other method, the freedom from hair-splitting judicial restraint, the unification of leadership, while not without its disadvantages and abuses as in the unnecessary suppression of freedom of speech, left an abiding impression of the possibilities of governmental reorganization in America, when unified social ideals and symbolism found free expression in public action. (p. 1539.)

VI

In the end, after considerable study and cogitation over these two large volumes, I come reluctantly to the conclusion that William Graham Sumner has himself become a "forgotten man." For in Section 102 of *Folkways* he stated, with devastating clarity and finality, the fallacy underlying such enterprises as seeing "where social stresses are occurring and where major efforts should be undertaken to deal with them constructively," which is what Mr. Hoover says in his foreword that *Recent Social Trends* should help us all to do. Section 102 is too long to quote in full here, I regret to say, but perhaps the following passage will suffice, and with it I am content to end this discussion:

When, however, the statesmen and social philosophers stand ready to undertake any manipulation of institutions and mores, and proceed on the assumption that they can obtain data upon which to proceed with

confidence in that undertaking, as an architect or engineer would obtain data and apply his devices to a task in his art, a fallacy is included which is radical and mischievous beyond measure. We have as yet, no calculus for the variable elements which enter into social problems and no analysis which can unravel their complications. The discussions always reveal the dominion of the prepossessions in the minds of the disputants which are in the mores. We know that an observer of nature always has to know his own personal equation. The mores are a societal equation. When the mores are the thing studied in one's own society, there is an operation like begging the question. . . . . It is vain to imagine that a "scientific man" can divest himself of prejudice or previous opinion, and put himself in an attitude of neutral independence towards the mores. He might as well try to get out of gravity or the pressure of the atmosphere. The most learned scholar reveals all the philistinism and prejudices of the man-on-the-curbstone when mores are in discussion. The most elaborate discussion only consists in revolving on one's own axis. One only finds again the prepossessions which he brought to the consideration of the subject, returned to him with a little more intense faith.

BRIEF NOTICES

EVOLUTION

Evolutionist and Missionary John Thomas Gulick. *Portrayed Through Documents and Discussions.*

By Addison Gulick. University of Chicago Press, Chicago. $4.00. 6x9; xvi + 556; 1932.

The material in this book falls into three parts: I. Youth and Early Travels; II. Productive Life; III. The Biological Evolutionist. The material is derived mainly from personal journals and letters, and family letters. It is skilfully edited and makes altogether an extremely interesting book. One gets first the colorful tale of early missionary activity in the South Seas; and learns, by the way, of the manner of the founding of some of the great Hawaiian fortunes. Then follows the story of *Wanderjahren* in pursuit of an education. Then the life as missionary, culminating in the years in Japan, with their profound and appreciated results. All along is the never ending struggle with ill health and the equally unfailing zeal for natural history. Altogether it was a great life, nobly lived.

After a summary but excellent analysis of Gulick's contributions to evolution, and their significance, the book ends with a bibliography, briefer than one would have supposed to have been the fact, and an index of 40 pages.

Altogether this is a notable contribution to biographical literature, and to the history of biology.

The Scientific Basis of Evolution.

By Thomas H. Morgan. W. W. Norton and Co., New York. $3.50. $5\frac{5}{8}$ x $8\frac{1}{4}$; ix + 286; 1932.

In this book one of the foremost living geneticists considers the bearing of modern work in genetics on the problem of evolution. The author's viewpoint is indicated in the following passage:

> It is, in fact, the main purpose of this book to insist that the study of evolution has become sufficiently advanced to rest our case for its acceptance on the same scientific procedure that has led to the great advances in chemistry and physics. Whether this procedure is called mechanistic or by some other name does not so much matter as does the recognition that only by experiment may we hope to rescue the theory of evolution from the vague speculative methods of its immediate past. It is mainly for this reason that I have in the last two chapters discussed the opinions of philosophers, metaphysicians, and mystics concerning organic evolution. My contention is that these speculations have not been helpful in finding out how evolution has come about. On the contrary, I think that these attempts to remove the problem from the biological field have done more harm than good, by their popular appeal to mysticism, and by directing attention away from the more laborious but safe procedure of studying the problem of evolution in the same way that other scientific problems are studied.

The Causes of Evolution.

By J. B. S. Haldane. Harper and Bros., New York. $2.50. $5\frac{1}{4}$ x $7\frac{1}{2}$; vii + 235; 1932.

In this book the author summarizes the genetic evidence on variation and interspecific differences and the work of Fisher, Wright and himself on the mathematical theory of natural selection. His conclusion is

> that natural selection is the main cause of evolutionary change in species as a whole. But the actual steps by which individuals come to differ from their parents are due to causes other than selection, and in consequence evolution can only follow certain paths. These paths are determined by factors which we can only very dimly conjecture. Only a thorough-going study of variation will lighten our darkness. Although we have found reason to differ from Darwin

on many points, it appears that he was commonly right when he thought for himself, but often wrong when he took the prevailing views of his time—on heredity, for example—for granted.

A Chronological Table of Prehistory.
By Miles Burkitt and V. Gordon Childe. Roland Austin, 24 Parkend Road, Gloucester, England. 2s. 6d. $7\frac{1}{8} \times 9\frac{3}{4}$; 22 + folding chart; 1932 (paper).

All the established facts from Eolithic times up to Julius Caesar and Roman times, are presented in tabular form. The tabular chart is divided into twenty-eight columns headed by geographical areas, covering the known prehistoric world. There is a twenty-ninth column headed "Climatic phases." These columns are divided on the vertical axes into Eolithic, Lower Palaeolithic, Middle Palaeolithic, and Upper Palaeolithic periods, followed by the calendar dates 3000 B.C. to 0, in approximately 200 year intervals. A brief discussion of prehistory accompanies and supplements the table.

Altogether the chart gives a sound and well-correlated picture of the stratigraphy of man's cultural evolution.

Contributions to Paleontology from Carnegie Institution of Washington. *Papers Concerning the Palaeontology of California, Oregon and the Northern Great Basin Province. Carnegie Institution of Washington Publication No. 418.*
Carnegie Institution of Washington. \$2.00 (paper); \$3.00 (cloth). $6\frac{3}{4} \times 10$; 113; 1932.

This monograph contains six descriptive papers: I. Distribution and Age of Marine Tertiary Deposits of the Colorado Desert, by W. P. Woodring; II. Distribution and Description of Skull Remains of the Pliocene Antelope *Spenophalos* from the Northern Great Basin Province, by Eustace L. Furlong; III. A Miocene Mammalian Fauna from Southeastern Oregon, by C. Lewis Gazin; IV. Additions to the Mammalian Fauna from the Tecuya Beds, California, by Chester Stock; V. A New Genus of Otter from the Pliocene of the Northern Great Basin Province, by Eustace L. Furlong; and VI. A Contribution to the Paleozoic Geology of Central Oregon, by E. L. Packard. All but the first and last of these papers are illustrated with photographs of specimens found.

GENETICS

Chromosomes and Plant-Breeding.
By C. D. Darlington. The Macmillan Co., New York. \$1.75. $5\frac{1}{2} \times 8\frac{1}{2}$; xiv + 112; 1932.

Recent Advances in Plant Genetics.
By F. W. Sansome and J. Philp. P. Blakiston's Son and Co., Philadelphia. \$4.00 net. 5×8; x + 414; 1932.

These two books were written by members of the John Innes Horticultural Institution. Darlington's book is intended to indicate to horticulturists the service cytology may render in the practical conduct of breeding experiments. He points to a long list of cytological studies, some of them his own, on cultivated plants in support of his conclusion:

> While chromosome studies therefore do not give the plant-breeder any great control over his material, they enable him to direct his efforts into the right channels for obtaining and preserving the results likely to prove most profitable to him.

There is a good index and the bibliography is complete enough for an introductory text.

We could not entirely suppress the suspicion that a considerable part of the recent advances in plant genetics must have been made by reading the *Drosophila* literature. Certain it is that the mechanisms of inheritance in the fruit fly have been taken over bodily in very many instances to fill in gaps in the plant data. This being so, it is difficult for an American biologist to conceive "the unfortunate lack of contact that exists at present between the plant and animal branches of the science" which Sansome and Philp hope to remedy with their book. The principal development of the last ten years peculiar to plant genetics appears to be a growing appreciation of the importance of polyploidy as a factor in the heredity of crop plants. As in work on *Drosophila*, the widespread application of cytological methods has altered

the whole aspect of the science during the last decade and this book gives an account of developments during a period of extremely rapid growth. The book is well indexed and its bibliography runs to more than 1200 titles. It should be very useful to geneticists.

HEREDITY *in the Light of Esoteric Philosophy.* *By Irene B. Hudson. Rider and Co., London.* 3s. 6d. net. $4\frac{3}{4}$ x $7\frac{3}{8}$; 144; no date (1932?).

For some time it has been apparent that biology is on the way to higher and better things. We suspect that it will not be long until physics begins to sweat to maintain its place as premier purveyor of pseudo-scientific mysticism to the intelleboobectuals. [This is a portmanteau word composed by Reginald the Office Boy in the Classical Dodgsonian tradition. In reading aloud pronounce each syllable slowly and clearly and put the accent on the fourth syllable from the start.] The author of the present treatise, while plainly neither an Eddington nor a Millikan in intellectual stature, is, however, like the proverbial organist, doing her best. What she sets out to do is to reconcile, or better to unite theosophy and modern genetical theory. After a chapter composed of quotations from T. H. Morgan, Crew, R. R. Gates, and others, she gets to grips with her evolution and philosophy. The result is really swell stuff. Lack of space alone prevents us from doing it justice. It reeks with gems of thought like the following:

> The anthropoid apes are the "degenerate descendants" of this renewal and conscious sin. They are truly "speechless men," and are *millions of years later than the speaking human being*. They will become speaking animals (or men of a lower order) in a later cycle of evolution, while the Adepts of a certain school hope that some of the Egos of the apes of a higher intelligence will reappear at the close of the next Root Race.

VERERBUNGSLEHRE. *Mit besonderer Berücksichtigung der Abstammungslehre und des Menschen. Bd. I. Mendelismus. Zweite Auflage.* *By Ludwig Plate. Gustav Fischer, Jena.* 28 marks (cloth); 26 marks (paper). $6\frac{1}{4}$ x $9\frac{1}{8}$; x + 554; 1932.

The first edition of this *Vererbungslehre* appeared in 1913. Since that time the literature on genetics has increased to such an extent that in bringing the book up-to-date the distinguished author has found it necessary to publish the second edition in three volumes. This, the first volume of the expanded work, deals with the elements of cytogenetics, cleavage, multiple allelomorphism, multiple factors, and chromosome Mendelism (linkage, crossing-over, Morgan's theory, polyploidy and aberrant chromosomes). The second volume, on sexuality and general problems, is in press. Each volume has its own bibliography and index. There is still a third volume in preparation. This will consider the special genetics of the animals which have been most thoroughly studied, and the eugenics of healthy and sick persons. Plate is a wise, forthright, and occasionally salty writer, who may be read with profit if not always with complete agreement. This book when completed will have to be a part of the reference equipment of every biological laboratory.

PRINCIPLES OF GENETICS. *A Textbook, with Problems. Second Edition.* *By Edmund W. Sinnott and L. C. Dunn. McGraw-Hill Book Co., New York.* $3.50. $5\frac{7}{8}$ x 9; xvi + 441; 1932.

This second edition of a well and favorably known text-book on genetics represents a thorough revision of the old text and incorporates results of recent investigations which have led to important new ideas. More emphasis is laid on principles. The three chapters in the first edition devoted to applications of genetics in agriculture and human heredity have been omitted from this edition. Seduced by the prevailing Genetical Uplift the authors have added two new chapters on the application of genetics to biological theory. There is a more detailed consideration of the physical basis of inheritance. Many topics of importance omitted in the text itself are called to the attention

of the student in a series of Reference Problems at the end of each chapter. A list of references also follows each chapter. A discussion of biometric methods is appended, and there is a full index.

Bud Variation in Peaches. *U. S. Department of Agriculture Circular No. 212.*

By A. D. Shamel, C. S. Pomeroy and F. N. Harmon. U. S. Government Printing Office, Washington. 10 cents. 6 x 9¼; 21; 1932 (paper).

This circular is a report on a scientific study of bud variation in the trees of several important canning varieties of peaches which was begun in 1925 and has been continued to the present time.

These studies include annual individual-tree performance records in plots where the cultural and other conditions seem most favorable for this work. A systematic effort is being made to determine varietal characteristics by means of estimate-yield records, together with careful notes and illustrations of outstanding foliage and fruit characters.

Progeny tests of the variations are being made. Improved strains for commercial use will probably be developed from some of the variations that are described in this circular.

The Genetical Factor in Endemic Goiter. *Carnegie Institution of Washington Publication No. 428. (Paper No. 37 of Department of Genetics.)*

By Charles B. Davenport. Carnegie Institution of Washington, D. C. 75 cents (paper); $1.25 (cloth). 6¾ x 10; iv + 56 + 4 folding charts; 1932.

Endemic goiter is usually attributed to environmental conditions. But, since in an endemic region not everyone has goiter, and the goiter which is found tends to be in particular families, the hypothesis is advanced that the environment merely brings out a thyroid insufficiency based on gene defects which would go unnoticed if the conditions were entirely favorable. An investigation was made on families in a mountain valley in Western Maryland, the details of which are presented in this publication. In regard to the genetical factor, the conclusions are that two coöperating genes do the job: one sex-linked and dominant; the other autosomal and dominant.

Mule Production. *U. S. Department of Agriculture Farmers' Bulletin No. 1341.*

By J. O. Williams. U. S. Government Printing Office, Washington. 5 cents. 6 x 9¼; 27; 1932 (paper).

An informative leaflet on the breeding and care of mules.

GENERAL BIOLOGY

Experimental Analysis of Development. *By Bernhard Dürken. Translated by H. G. and A. M. Newth. W. W. Norton and Co., New York.* $4.75. 5⅝ x 8¾; 288; 1932.

In this translation from the German, an excellent account is given of the present status and current major problems of analytical embryology. Following a consideration of methods of approach, the major problems are outlined as follows: 1. The determination of the *limits of potency* (of the uncleaved egg and its separate parts, of blastomeres, and organ rudiments) at different periods of development. By potency is meant the primary developmental capacity of the germinal region in the egg, which transcends the actual fate of the zygote. 2. *Regulative phenomena:* the production of a normal whole, following loss or change in one part of the developing organism. 3. *Determination of parts:* the narrowing down of the extensive potentialities of the germinal regions to what they will actually perform. 4. *Processes of realization* following determination processes: environment functions here as well as inherited factors. The problem arises as to whether environment has only individual, or also transindividual action. 5. Problems concerning the extent to which *interrelations* and *modifications* of the parts of the whole organism are functions of chemistry, energy-relations, etc. 6. Relative competence of the *genetic* and the *embryological approach* to deal with the problems of the internal factors in develop-

ment. 7. The importance of the *whole* organism in the process of development.

After this survey of the present fields of investigation, fertilization is considered. It is shown that the male and female reproductive cells are equivalent to one another, and that the essential in the process of fertilization is not the activation of the egg, but rather the union of two separate systems, very similar as regards their potency, to form a new individual. This union is not a mosaic-like apposition of two systems, but is the origin of a new unit and whole. This fusion reveals the presence of a specific organismic faculty which cannot be referred to any organization either mechanistically or morphologically explicable.

The remainder of the book is devoted to a discussion of the nature of development. Development is regarded as carried out by a special *reaction-basis*—the name given to the whole of the specific constitution of the germ cell, including those of its primary morphological differentiations which are essential to its development. The reaction-basis is the actual bearer of all the inherited internal factors of development. It does not contain a preformed particle of protoplasm corresponding to each single part of the resulting individual.

> It is more true to say that the egg—i.e. the individual in its unicellular condition—owes its general determination as regards purely specific and racial peculiarities to the reaction-basis, while determination of the morphological value of the separate parts follows step by step. The solution of the problem of the specific and racial determination of the whole organism would therefore involve an investigation of the real nature of the reaction-basis. Experimental embryology, as an analytical science, cannot, however, argue from the whole to its parts, but must arrive at a comprehension of the whole through understanding the parts. Hence .... the question of the determination of the parts is the essence of the determination problem. This determination comes about by degrees, earlier or later according to the kind of animal in question, so that an indeterminate condition gradually gives place to a determinate one. .... Not only does it lead little by little from the general to the particular, but the rigidly determined condition is connected by intermediate stages with the indeterminate condition, beginning with the first appearance of determination—when it is still indefinite—and proceeding to its final complete establishment.

In the final chapter, some of the difficulties which arise when the chromosome theory, with its rigid materialistic determinism, is considered in the light of the actual phenomena observed in experimental embryology, are discussed. It is concluded that

> .... the primary foundation of the reaction-basis is not a mosaic of discrete parts. It is the totality of the germ-cell, to which the individual constituents distinguishable in the cell are subordinated—whether these constituents can be passed on to the descendants more or less directly, or whether they must be reformed at the beginning of each new development, with the whole specific constitution of the reaction-basis as their starting-point. Development is Epigenesis.

EMIGRATION, MIGRATION AND NOMADISM. *By Walter Heape. Edited with a Preface by F. H. A. Marshall. W. Heffer and Sons, Cambridge.* 12s. 6d. net. $5\frac{1}{2} \times 8\frac{1}{2}$; xii + 369; 1932.

A book of deep interest to biologists. Its distinguished author did not live to see his book through the press, but that work has been ably done by F. H. A. Marshall, who also contributes a preface. In a lengthy introduction Heape outlines the growth of his ideas concerning the physiology of the reproductive system (which he believes to play a far more important part in the history of evolution than is generally recognized), the interrelations of the digestive and the reproductive systems, the cumulative effect of the gonadic secretions, the probable part played by vitamines on the growth and on the breeding excitant of animals, the causes leading up to the movements of animals from one territory to another, etc. The sections following the introduction are as follows: Territory; Emigration (three chapters); Diffusion, dispersal and drift emigration; Migration (two chapters); Hibernation and aestivation; Nomadism, and Conclusion.

The author defines the nature of the different kinds of voluntary movements of animals, drawing a sharp distinction between the terms emigration (permanent evacuation of home territory) and migration. He believes that

> "the conception of the possession of territory or of property is inherent in all animals capable of voluntary movement from place to place, that territorial rights are universally recognized and almost always strictly respected by all animals except 'raiders,' "

and that while territorial rights extend only over limited areas there are huge tracts of neighboring country which are clearly recognized, except by predaceous animals, as neutral territory. Incentives to individual movement are classed as alimental, climatic, and gametic. These arise from quite different physiological influences. The combined effects of excessive reproduction over a definite tribal area and the consequent scarcity of food which leads to mass movements are extensively discussed. The source of the impulse to migrate for breeding purposes he suggests is derived from "the same gonadic secretion, which I called 'gonadin,' that is responsible for the growth of the secondary sexual characters, which also precedes sexual activity."

He is inclined to believe that

> "the origin of what I have called an epidemic of hysteria will also be found to be associated with some pathological change in an organ of the reproductive system. The simultaneous exhibition of this hysterical condition in all the members of a large number of herds occupying a definite territorial area is a very remarkable incident. I imagine it may primarily be due to a change in the quality of the food supply of that area; and I hazard the suggestion that the normal functional activity of the gonads is thereby interfered with, either unduly excited or checked."

The frequent selection of unfavorable routes by mammals undergoing mass emigration which ultimately lead to death, is possibly due to the fact that they choose the only route available if the rights of territory of others are to be respected. The author gives in the final chapter a brief note on Evans' and Burr's work (1925). The work concludes with a lengthy bibliography and an index.

Problems of Relative Growth.

By Julian S. Huxley. The Dial Press, New York. $3.50. 5½ x 8⅝; xix + 276; 1932.

This book is a useful review of the literature on the differential growth of the parts of organisms and related topics. It is very fully and well illustrated, documented, and indexed. On these accounts it will be of service to all students of the problems of growth. In respect of the ideas which it embodies the book owes a very great deal to D'Arcy Wentworth Thompson, to whom it is appropriately dedicated. The material is organized and presented with great skill. The general conclusions reached are:

> Starting from the fact of obviously "dysharmonic" or heterogonic growth, we have discovered our first new empirical law—the law of constant differential growth-ratio. We have then recognized that it is only a special case of the law of differential growth-partition, which is the prime quantitative basis of relative growth. Passing on from that, we have found a further and quite unexpected empirical law—that the existence of a differential growth-ratio in an organ or region seems always to be associated with a growth-gradient culminating in a growth-centre; or in other words, that the distribution of growth-potential is not marked by discontinuities or by frequent oscillations, but occurs in an orderly and continuously graded way. And we then showed that these localized growth-gradients were but special cases of growth-gradients permeating the whole body. These laws, however, only appear to apply to the stages of growth occurring after histological differentiation has been completed. Very rapid growth, obeying quite other laws, occurs during the earlier period. For these two phases of development, the terms histo-differentiation and auxano-differentiation are proposed.

Riddles of Science.

By Sir J. Arthur Thomson. Liveright, New York. $3.50. 5¾ x 8⅜; 387; 1932.

Although this is written for the layman the author covers a wide range of subjects, with lucidity and an admirable scientific caution. Any chapter, picked at random, proves a complete and entertaining whole. The subjects are for the most part presented in the form of a question, an effective manner to catch the attention of the general reader. The first part deals roughly with general physiological riddles ranging from such different questions as "How does life begin?," "Why must we die?," to "What are hormones?," "Why do we laugh or cry?," "Why does your hair turn grey?," etc.

Part II deals with problems of natural history, such as "Riddles of the country side," insects, galls, the homing instinct, and "Natural wireless" which leads directly into the third part in which the author attacks psychological phenomena. We cannot but respect his unprejudiced treatment of telepathy, clairvoyance and

crystal gazing. In Part IV the author discusses Evolution, and what is behind it all. There is a charming epilogue on the "Wonders of the world."

The book is highly to be recommended as a thoughtful, intelligent and conservative explanation of many of the questions which occur to the inquiring mind. There is no index.

MOVEMENT AND LOCALIZATION OF THE PRESUMPTIVE EPIDERMIS IN TRITURUS TOROSUS (RATHKE). *University of California Publications in Zoology, Vol. 36, No. 13.*

By A. Mandel Schechtman. University of California Press, Berkeley. 25 cents. 7⅛ x 10¾; 22 + 6 plates; 1932 (paper).

This contribution to the study of developmental mechanics in the amphibia is based on the application of the Vogt method of vital staining to embryos of *Triturus torosus*, the common newt of the Pacific Coast. Stains are made on different localities of embryos of different stages, and their fate followed as the embryo develops. Among the results, which are presented in summary, are the following:

> Marks made on the germinal area (*Richtungsfleck*) appear on or adjacent to the anterior margin of the medullary plate. Presumptive epidermis and medullary materials are contiguous in the region of the animal pole as early as the zygote stage. Presumptive epidermis occupies approximately the ventral half of the embryo in the slit-shaped blastopore stage; presumptive medullary material occupies the remaining dorsal half.

The progress of the presumptive epidermis of tail, caudal fins, head, mandibular arch and brachial area is also indicated.

RECENT ADVANCES IN CYTOLOGY.

By C. D. Darlington. P. Blakiston's Son and Co., Philadelphia. $4.00. 5⅛ x 7⅞; xviii + 559; 1932.

In the preface the author states that the

> present work attempts to describe one aspect of cytology, the study of the nucleus and the chromosomes in plants and animals. It consists of three elements: an introduction for the student who is a beginner, a résumé for the research worker who requires classified observations, and a theoretical treatise, in which my own views are developed, for the general biologist.

Students and investigators will find this a useful book. The work has been done conscientiously. Many will disagree with the author's interpretation of previous morphological studies of nucleus and chromosomes and attack his theories as unsound or obscure. Nevertheless his views are entitled to consideration, particularly by the research worker and the general biologist, who cannot fail to find many of his hypotheses conducive to new points of view. The book is well documented and illustrated. In a group of four appendices he discusses cytological interpretations, and recent improvements in technique, and gives a glossary and lengthy bibliography. J. B. S. Haldane contributes a foreword. There is a subject index.

NONSUCH: *Land of Water.*

By William Beebe. Brewer, Warren and Putnam, New York. $3.50. 5⅞ x 8⅝; xv + 259; 1932.

In this group of essays Doctor Beebe tells with his usual charm of the animal and plant life, marine and terrestrial, of Bermuda. We follow him in his underwater adventures on the shoals and reefs; we watch the behavior of the peacock flounder with its periscope eyes and the birth of the young seahorses from the pouch in which their father has incubated them. Other interesting essays deal with the cedars and how they came to Bermuda, with the migration of birds and lemmings and eels, with sharks and crabs and snails. This is the first of a series, one of which is to describe the author's observations on the life of the deep sea, while others will be devoted to the life histories of Bermuda fish. There is an index.

BIOLOGY. *An Introduction to the Study of Life.*

By H. Munro Fox. The Macmillan Co., New York. $1.75. 4¾ x 7¼; xv + 344; 1932.

This little book is designed primarily for elementary and high school teaching, hence the presentation is simple with a

minimum of technical detail. The author adopts the method of teaching whereby one begins with man and ends up with fossils. We question the advisability, however, of introducing a student immediately to physiological problems of respiration, digestion and circulation; further, it is questionable if he gets a very clear conception of the actual evolutionary sequence from simple forms to complex ones. Apart from this criticism, there is much to recommend this book; the author appreciates the value of stimulating a naturalistic feeling for biology, and gives many suggestions for simple and interesting experiments that any young student can perform by himself.

Elements of Biology.

By C. von Wyss. With a Foreword by Sir J. Arthur Thomson. Christophers, London. 6 shillings net. 5 x 7⅞; xvi + 326; 1932.

We take pleasure in recommending this charming and accurate introduction to the study of biology. Although this book was written primarily for children, adults who wish to familiarize themselves with this subject will find it interesting and stimulating. Miss von Wyss begins the book with the march of the seasons; then goes on to the process of living, the fitness and progress in living, and the relation of organisms to their environments; and ends it with a chapter citing instances in which man's knowledge of the biology of plants and animals has aided in his welfare.

A Survey Course in General Biology.

By James G. Needham. Comstock Publishing Co., Ithaca, N. Y. $2.70. 5¼ x 7½; vii + 376; 1932.

The book is planned for those who are not specializing in biology, hence controversial matters, recondite theories, and discussions of animals with which the student may not easily familiarize himself are omitted. The author sticks to the conventional pedagogic order of exposition; that is, from the simpler forms to the complex. In this way he succeeds in emphasizing the logic of the science of biology, which it seems, at present, to be the fashion to ignore in biological teaching. An excellent text, highly recommended.

Fundamentals of Biology. *Second Edition.*

By Arthur W. Haupt. McGraw-Hill Book Co., New York. $3.00. 5¾ x 9; x + 403; 1932.

The second edition of this useful textbook follows the same conservative presentation of material as the first (reviewed here in Volume IV, pp. 265–266). Emphasis is laid rather on cultural aspects than technicalities, as the book is designed for elementary courses. Nevertheless the fundamental facts of both botany and zoology are soundly and interestingly presented.

HUMAN BIOLOGY

Caste and Race in India.

By G. S. Ghurye. Alfred A. Knopf, New York. $4.00. 6 x 9½; vii + 209; 1932.

This book, written by an Indian of high scholarly attainments, will find a wide circle of interested readers. The author shows that there is nothing mysterious or sacred in the institution of caste. It is simply a highly exaggerated variation of the social differentiation which has existed from time immemorial amongst groups of societies throughout the world. The rigidity of this particular system is due to the fact that caste membership depends upon birth and that each group is governed by its own minute rules as to religious and social customs, diet, etc. There is a definite scheme of social procedure among the castes, the Brahmin standing at the head of the hierarchy and the untouchables falling into the very lowest group, with numerous classes and subclasses in between the two. Mr. Ghurye has nothing to say in favor of the present caste system. Neither does he see a favorable solution of the problem in the near future. He shows in a general survey of caste development from earliest historical to modern times how the present extremely complicated and evil situation has

naturally developed, and discusses the various methods which have been proposed to either abolish or modify its strangling hold on Indian peoples. He believes it the duty of every educated and progressive Hindu leader to ignore caste. Possibly the greatest blow to it will come from the educated young men and women of India who insist upon freedom in marriage.

Anthropologists will be interested in his section on Race and Caste in which he analyzes and compares bodily measurements made on racial and caste groups of Indians. In an appendix he gives these measurements in tabular form. The volume is well documented and indexed.

THE CHANGING CULTURE OF AN INDIAN TRIBE.

By Margaret Mead. Columbia University Press, New York. \$4.50. $5\frac{7}{8}$ x 9; xiv + 313; 1932.

Scientific investigations of the American Indians have heretofore been confined mostly to a recording of what their aboriginal cultures were before and during the early period of their contact with that of the white man, and what has happened to them since has been neglected by the student of culture history. Dr. Mead spent four months on a reservation in the Mississippi Valley, and in this book gives an account of the disintegration and partial reintegration of the tribe which she here calls Antler. She pays particular attention to the Indian woman in transition, and this book may be considered as a contribution to the study of woman in general.

Little remains of the Antler's former culture. However, he has not as yet been very successful in adjusting himself to that of white society, especially its economic behavior. This is particularly true of the man.

> The social elaborations of gens, chieftainship, society, war police, have vanished, to leave only the household and the social dancing lodge; it is the women who are now the core of Antler culture. It is the women who are able to teach their daughters the dancing steps, the household arts, which are all that are left of the culture. The men are Indian by virtue of blood, language, and a disinclination to accept the economic behavior and economic attitudes of white society. But the women are still Indian in positive terms, in a multitude of details which bind mother to daughter and both to the grandmother.

An appendix contains tabular and diagrammatic treatment of raw materials, including household organization, marital situation, case histories of delinquent girls and women, and sample conversations. The book has an index but no bibliography.

A PRELIMINARY STUDY OF THE RUINS OF COBÁ. QUINTANA ROO, MEXICO. *Carnegie Institution of Washington Publication No. 424.*

By J. Eric Thompson, Harry E. D. Pollock and Jean Charlot. Carnegie Institution of Washington, D. C. \$4.50 (paper); \$5.50 (cloth). 9 x 12; vi + 213 + 12 plates + 6 folding charts; 1932.

Cobá, one of the largest of the known Maya cities, is situated in Mexico close to the Yucatan border in a region far more favorable to colonization than is usually to be found in the interior of the Yucatan Peninsula. A series of small lakes furnishing a permanent water supply, an abundant rainfall, and an almost tropical vegetation, undoubtedly made this a highly desirable habitat for the Mayas. The date of the destruction of the city is unknown, although some brief historical notes possibly indicate that it was around 1212 A.D. Since 1926 several expeditions have been sent out by the Carnegie Institution to Cobá and the vicinity. In this volume are recorded the results of these studies. The *Introduction* is by J. Eric Thompson. Harry E. D. Pollock contributes the next two sections on *Description of the Ruins* and *Architecture*. The fourth section is by Mr. Thompson on the *Monuments of the Cobá Region*, and this is followed by *Art Analysis of the Macanxoc Stelæ*, by Jean Charlot. In the final chapter Mr. Thompson discusses what conclusion can be drawn at present concerning the importance of Cobá as a cultural center and its influence and relations with other cities to the eastward and in Northwest Yucatan. He points out that in the past "too many outlines of Maya history have been built up on a very slender basis"

and that only when extensive studies of Maya ceramics and architectural developments have been made can Maya history be reconstructed. Excavations when undertaken at Cobá may possibly furnish many clues now missing.

The volume is issued in the usual very excellent format of these publications and contains excellent maps and reconstruction diagrams, also numerous very fine photographic reproductions. It is well documented and indexed.

EMPLOYMENT OF MENTALLY DEFICIENT BOYS AND GIRLS. *United States Department of Labor, Children's Bureau Publication No. 210.*

By Alice Channing. U. S. Government Printing Office, Washington. 15 cents. $5\frac{7}{8} \times 9\frac{1}{8}$; v + 107; 1932 (paper).

This is the report of a study made to determine the industrial adjustment of mentally deficient boys and girls after they leave the special classes in the public schools or the public institutions for the feeble-minded. Part I deals with former special-class pupils in Newark, Rochester (New York), Detroit, Cincinnati, Los Angeles, San Francisco and Oakland. As a rule, the I.Q. of these pupils was below 75. The interval between the date they had left the school and the date they were interviewed ranged from three to seven years. In all, 1,067 former pupils were investigated. The group studied is discussed with regard to sex, economic condition of families, I.Q.'s, physical defects, school progress and delinquency records. The information in each case is summarized in tabular form. Entrance upon working life is then considered, and the continuity of employment, occupations undertaken, wages received and success in jobs. The various topics are illustrated with case-history material. The results of the whole study are summarized and conclusions drawn. The need for the development of a system of placement and supervision for pupils from special classes is indicated.

Part II presents a similar study made on boys and girls formerly in Illinois State Institutions for the Feebleminded. The indications are that boys from the institutions did not have as favorable work experiences as those from the special classes. A much larger number had serious court records for delinquency. This fact points to the great need for follow-up work for those leaving the institutions.

CRIMINOLOGY.

By Robert H. Gault. D. C. Heath and Co., Boston. $3.48. $5\frac{7}{8} \times 8\frac{3}{4}$; ix + 461; 1932.

Gault puts great emphasis on the psychological and pathological approach to the study of criminology. He believes that the greatest sources of our behavior are acquired attitudes which develop out of infinitely numerous reactions to our environment, these reactions depending upon native capacity, prepotent reflexes, and other influences. Numerous case histories, particularly those of the young, are given and the development of criminal attitudes is traced as they arise through unfortunate home influences, evil companionship, or other adverse social contacts. The book is divided into two sections. Under the heading *The criminal personality* we find such subjects discussed as personality, emotion, intelligence of criminals, psychopathic personality, epilepsy, race and sex, attitudes, from the gang to organized crime, and heredity in relation to criminality. The second part, *The struggle against crime*, deals with institutional and extra-institutional treatment of criminals, methods of obtaining evidence, and preventing the development of criminals. In a series of three appendices are discussed training courses for prison and police officers, programs of criminologic research institutes, and a plan for a crime prevention bureau. The book contains a number of tables, literature lists at the conclusion of each chapter, and an index. Jerome Davis has written an introduction.

PROSPECTING FOR HEAVEN. *Some Conversations About Science and the Good Life.*

By Edwin R. Embree. The Viking Press, New York. $1.75. $5 \times 8\frac{1}{8}$; 185; 1932.

The physical sciences have given us a control over our environment much greater

than our forefathers possessed, yet we are still far from satisfied with our own lives. In this symposium the author gives his version of what may be expected of the mental sciences towards a happier and more satisfying life. C. M. Hincks, Medical Director of the United States and Canadian National Committees for Mental Hygiene, tells what is being done for the cure of the insane and the adjustment of the feeble-minded to their environment; Victor G. Heiser, Director for the Far East of the health work of the Rockefeller Foundation, describes the achievements of medical science; Franz Alexander, the distinguished psychoanalyst, presents the contribution of his subject towards sane living; Charles H. Judd, Director of the School of Education of the University of Chicago, tells of the rôle of education in preparing the individual for life; and Howard W. Odum, Director of the Institute for Research in Social Science of the University of North Carolina, describes the contribution which sociology may make towards a more satisfying social order. While the conversations did not take place in precisely the form recorded in the book, the members of the symposium accept them "as conveying accurately some at least of our ideas as to possible scientific steps to the good life." There is no bibliography or index.

THE TRIAL OF JEANNE D'ARC. *Translated into English from the Original Latin and French Documents, by W. P. Barrett. With an Essay* On the Trial of Jeanne d'Arc *and* Dramatis Personae, *Biographical Sketches of the Trial Judges and other Persons Involved in the Maid's Career, Trial and Death, by Pierre Champion. Translated from the French by Coley Taylor and Ruth H. Kerr.*

Gotham House, New York. $4.00. 6¼ x 9¼; xiii + 544; 1932.

This is the first complete translation into English of the official record of the trial of Jeanne d'Arc. The historian and the student of mystic phenomena and of witchcraft will find in it valuable material, while the general reader cannot but admire the fortitude of the peasant girl of nineteen, without counsel, and pitted against so many subtle theologians. Champion in his discussion of the trial agrees with Anatole France as to the partiality of the judges, and emphasizes the great share which the University of Paris, then the chief theological authority of the church, had in urging on the prosecution. In reading the trial record one cannot but wonder at the subsequent canonization of Jeanne. Her constant appeal is from the Church Militant to God. In short, Shaw's interpretation of her as the first Protestant seems to have much in its favor. The book has a bibliography of four pages, but no index.

MISCHIEFS OF THE MARRIAGE LAW. *An Essay in Reform.*

By J. F. Worsley-Boden. Williams and Norgate, London. 21 shillings net. 5½ x 8½; 427; 1932.

This is a somewhat dull, but extremely sound and solid legal treatise on the evolution, anatomy, and pathology of English marriage laws, civil and canon. Patiently, thoroughly and unemotionally the author lays bare in a devastating manner the absurdities of the English attitudes, as congealed into law, regarding marriage and divorce. He is, to be sure, *au fond*, a reformer and uplifter. He wants something done about it. But if all uplifters were as scholarly, patient, temperate, and fair as Dr. Worsley-Boden their critics would be largely disarmed. The essence of the reform advocated is simple and reasonable. It involves

> a definite rejection of the ecclesiastical view, as that view has been inherited from the long reign of the Papal canon law. It attributes the failure and unreality of the present law of England to the undue influence of the canon law in principle and practice; and, incidentally, it carries the contention that the ecclesiastical view, as expressed in the indissolubility of marriage, is not the best expression of the Christian religion.

BUT FOR THE GRACE OF GOD.

By J. W. N. Sullivan. Alfred A. Knopf, New York. $2.50 net. 5 x 7½; 220; 1932.

This entertaining book constitutes, among other things, a case history worthy of careful study by the human biologist. J. W. N. Sullivan, whose autobiography it is,

is a remarkable man. With a thorough, profound, and wide-ranging knowledge of mathematics and physics, and quite unable to be happy if long away from the atmosphere of the research laboratory, his outstanding achievement has been as a popularizer of the most recondite fields of mathematical physics. With all the essential equipment in the way of innate ability and technical knowledge far beyond that of many an F.R.S. he has never been a productive researcher. The reason, in his own words, is: "I had no creative ability, either as a writer or as a man of science."

The book is equally revealing about practically every other aspect of the author's life. This is what makes it so superb a case record. His amorous adventures, his passion for music which had as one result the writing of one of the best books on Beethoven ever produced, his spiritual restlessness, are all exposed and searchingly analyzed. This is a book which every young biologist starting his career should read. It lacks an index.

Roman Britain. *The Objects of Trade.*
By Louis C. West. Basil Blackwell, Oxford. 5 shillings net. $5\frac{1}{4} \times 8\frac{1}{2}$; iii + 108; 1932.

This little book contains in summary form a complete account, so far as the records show, of articles of trade and industry of Roman Britain covering the period between the time of Claudius and the fourth century. In each section the author discusses briefly the types of objects and their use and then in tabular form lists the object, its source, where found and authority. The objects exported range from forest products and cultivated plants through sea foods, pottery and metals to building stone. It will surprise many to learn that the British Isles produced precious and semiprecious stones. From the river mussels came pearls which, although of no very great value, apparently were much desired by the Romans. Pottery was imported in great quantities as were also wine, oil, bronzes and glassware. The author includes a list of British and foreign traders of the same period.

Digressions of a Man of Science.
By Sir A. Daniel Hall. Martin Hopkinson, London. 7s. 6d. net. $5\frac{1}{8} \times 7\frac{5}{8}$; 223; 1932.

In reading *Digressions of a Man of Science* we can easily imagine ourselves seated in a comfortable chair listening to Sir Daniel Hall speak in a pleasant, roaming fashion of his ideas and interests. These range from a scientific attitude towards faith to the culture of tulips. His primary interest, though, is in the research field of agriculture, its value and again its inconsistencies. He says that "the state must have research in order to obtain efficiency, but does mankind really care about efficiency?" Our author answers negatively and says man only wants to "loaf and possess his soul." This attitude is carried out in the book as the writer's various mental hobbies are treated with easy but pleasant lack of continuity. Writing is his digression and reading he would like to make yours.

The Causes of War. *Economic, Industrial, Racial, Religious, Scientific and Political.*
By Sir Arthur Salter, Sir J. Arthur Thomson, G. A. Johnston, Alfred Zimmern, C. F. Andrews, Frederick J. Libby, Henry A. Atkinson, Wickham Steed and Others, as Rapporteurs of the Various Sections of Commission I. of the World Conference for International Peace Through Religion—as Submitted to the Executive Committee for Presentation to the World Conference. With Introduction by Ruth Cranston. Edited by Arthur Porritt. The Macmillan Co., New York. \$1.50. $5\frac{1}{2} \times 7\frac{3}{4}$; xxix + 235; 1932.

This report is confined to an exposition of the causes of war and the tendencies that make for war. Probably no great war in the past has been due to a single cause, and the most apparent has not always been the most fundamental. Political and economic factors, which are now the most important factors leading to war, are especially intertwined. Concerning future wars we quote from Mr. Steed:

> The feeling of insecurity, and the fears which it engenders, are undoubtedly the strongest potential causes of war in the world to-day. No nation,

whether it belong to the League or not, and no signatory of the Paris Peace Pact, can be certain that, if it reduces its armaments to a point at which it would have to rely upon the help of others for defence against attack, such help would really be forthcoming.

On the Aboriginal Inhabitants of the Andaman Islands.

By Edward H. Man. With Report of Researches into the Language of the South Andaman Island, by E. J. Ellis. Royal Anthropological Institute, London. 8s. 6d. + 6d. for postage. $5\frac{3}{4} \times 8\frac{3}{4}$; xxxii + 254; 1932.

This is a welcome reprint of one of the classics of anthropology and ethnology, for a long time not readily accessible in its original form. Edward H. Man was Assistant Superintendent of the Andaman and Nicobar Islands, and resided among the aboriginal inhabitants from 1869 to 1880. His account of them was originally published in 1885 in the *Journal of the Anthropological Institute of Great Britain and Ireland*. It is a fine piece of work, systematically touching upon every aspect of the native lives, customs, habits, somatology, physiology, etc. The author's keen powers of observation were supplemented by a sympathetic insight into native ways of thought, and tolerance of differences of outlook and habit rare among officials, even to this day. Altogether it is a great service to anthropology to make this work available in separate form. It is well documented and indexed.

The Lame, the Halt, and the Blind. *The Vital Rôle of Medicine in the History of Civilization.*

By Howard W. Haggard. William Heinemann, London; Harper and Bros., New York. 21 shillings net (England); \$4.00 (U. S. A.). 6 x 9; xxiv + 420; 1932.

The subject of this book is the influence of medicine on civilization.

> Medical history is world history. Some phase of medicine has been involved in every great historical event, but usually these medical aspects have been ignored or overlooked. Consequently, when you turn to them they take you away from the beaten path of history and lead you instead into little-known byways of history. Yet, for everyone, medical history is probably more important than any other phase of history, for medical history discloses the forces that have made our modern civilization possible.

The thesis is developed through narrative, copious anecdotes, and delightful illustrations. The book is a worthy successor to the author's now famous *Devils, Drugs and Doctors.*

Fundamental Administrative Measures in Physical Education.

By Frederick R. Rogers. The Pleiades Co., Newton, Mass. \$2.75 net. 6 x 9; xvi + 261; 1932.

Decidedly one of the most sensible treatments of the subject that has appeared since physical education has attained academic recognition. The author has reviewed the field thoroughly and presents in addition a lucid philosophical discussion of the value of anthropometric measurements. We like his attitude towards physical education as expressed in the following:

> Joy is a great immediate health tonic. It is even possible that the total effects of health and vitality of a game of checkers played with intense enjoyment will be more beneficial than a basketball battle "played" under protest in a spirit of rebellion and hate.

Man Comes of Age.

By John Langdon-Davies. Harper and Bros., New York. \$3.50. $6 \times 9\frac{3}{4}$; x + 265; 1932.

As usual, our author has a great many words to say but perhaps it takes a good many to tell us what science has done to our philosophy and attitude towards daily life, and what science does or will do to settle the perplexities of existence. He tends only to present the problem, which of course has been done many times. Science can account for matter but not altogether for human behavior, for he admits we are of a "naughty world."

Wild Oats.

By Eric Muspratt. Gerald Duckworth and Co., London. 8s. 6d. net. $5\frac{1}{4} \times 8\frac{1}{2}$; 237; 1932.

This extraordinary book, written in the most approved realistic manner, with all the shocking words spelled out in full, tells the story of the author's adventures and his thoughts about them in bumming his way from England through France, Italy, Austria, Hungary, Germany, and Holland, and back to England. "Bumming" is the correct word. Mr. Muspratt plainly likes the life of a hobo, and perhaps likes still better to tell about it. He writes with considerable skill, and is robustly pleased with himself. The result is a significant social document which is also an entertaining book.

WELFARE OF CHILDREN OF MAINTENANCE-OF-WAY EMPLOYEES. *U. S. Department of Labor, Children's Bureau Publication No. 211.*
By Helen R. Wright. U. S. Government Printing Office, Washington. 15 cents. $5\frac{3}{4}$ x $9\frac{1}{4}$; v + 192; 1932 (paper).

A report of a field study, carried out in different parts of the United States, on the income, expenditures and living conditions of families of section-workers on the railroads. 550 families with 1,674 children comprise the group studied. The field work was completed in 1929, before lower wages, part-time employment or no employment reduced the family income, but even so the report presents a picture of insufficiency.

JUVENILE-COURT STATISTICS, 1930. *Based on Information Supplied by 92 Courts. Fourth Annual Report. United States Department of Labor, Children's Bureau Publication No. 212.*
U. S. Government Printing Office, Washington. 10 cents. 6 x 9; iii + 69; 1932 (paper).

This report consists of three parts: I. General discussion and summary tables; II. Comparative delinquency rates for 1930 and the 3-year period 1927–1929; III. Source tables. In courts having jurisdiction over children up to 18 years of age, 16 and 17 year old children were most frequently delinquent. Stealing and acts of carelessness or mischief were the most usual offenses of boys, whereas running away, being ungovernable, and sex offenses were most common among girls.

THE RACES OF MAN. *Differentiation and Dispersal of Man. Physical Anthropology.*
By Robert B. Bean. The University Society, N. Y. 6 x 9; vi + 134; 1932 (paper).

This little book traces some of the steps in man's ascent and the evolution of special attributes, points out the main routes of race dispersal and describes briefly the characteristics of the chief races and their subdivisions. There are suggestions for further reading, a glossary and an index.

THE SOCIAL SELECTION OF HUMAN FERTILITY. *The Herbert Spencer Lecture Delivered at Oxford 8 June 1932.*
By R. A. Fisher. Oxford University Press, New York. 70 cents. $4\frac{1}{2}$ x $6\frac{7}{8}$; 32; 1932 (paper).

In this lecture Fisher again argues in favor of a system of family allowances to counterbalance the effect of the social promotion of the less fertile and the consequent association of ability with infertility.

ZOÖLOGY

A NATURALIST IN THE GUIANA FOREST.
By R. W. G. Hingston. Longmans, Green and Co., New York. \$5.00. $5\frac{1}{2}$ x $8\frac{1}{2}$; xiii + 384; 1932.

This book is primarily an account of a novel and unique bit of zoölogical exploration, namely the study of the fauna of the tree-tops of a tropical forest. British Guiana was the *locale*, and the expedition directed by the author, Major Hingston, the distinguished English entomologist, went out under the auspices of the Oxford University Exploration Club.

The problem was to establish observation posts in the tree-tops and collect and study from them the inhabitants of the forest canopy. This was no easy matter. The average height of the roof was about 100 feet. Climbing that big a tree, under the conditions imposed by a tropical for-

est, is not done without taking thought. The expedition took out all sorts of gear from home, much of which proved in the end to be useless in practice. The native Indians really turned the trick for them; carrying up ropes with the help of climbing irons, and taking the first steps to rig blocks and tackles with which observation chairs could be run up and down.

As a piece of pioneering the work was a great success.

We were fairly satisfied with these rough efforts to study the animal life of the canopy. Apart from observations on the habits of the species—which constituted our main objective—we secured from the roof specimens of about 2,000 animals and 4,000 sets of plants. We fully realized, however, the primitiveness of our methods. The job was being done for the first time, and when leaving England we had only vague ideas of the way in which it ought to be tackled. We just brought along a heap of miscellaneous gear and made use of the contrivances that turned out most serviceable. That is the way of learning the first steps in an operation, and the experience gained has naturally exposed its rudimentary character and many imperfections.

The book is divided into two parts, both beautifully and effectively illustrated. The first part gives a running narrative of the expedition and a superb brief description of the general biology of a tropical forest. The trees make up

a selfish mob of ruthless competitors, every individual elbowing its companion out of the way, seizing and clinging to the least opportunity, until in the end a few of the most favoured ones pushed themselves as conquerors through chinks in the canopy. . . . The whole spectacle of forest within forest was a wonderful example of riotous struggle.

The second part is a series of essays on the natural history of various forms of life encountered, particularly spiders and insects.

Altogether it is a notable contribution to current biological literature. We recommend it warmly to our readers. It has a good index.

An Introduction to Zoölogy *Through the Study of the Vertebrates with Special Reference to the Rat and Man.*

By Zeno P. Metcalf. Charles C. Thomas, Springfield, Ill. \$3.50. $6\frac{1}{8}$ x $9\frac{1}{4}$; xix + 425; 1932.

This textbook departs from the more customary methods of introducing zoölogy to college freshmen. Instead of presenting a series of animal types starting with protozoa and ending with man, the author chooses one vertebrate, the rat, to be studied in detail so that the student may see how structure and functions are related. The book divides into three parts: (1) A general introduction, concerned with a summary of the various branches of zoölogy, and a brief classification of the animal kingdom; (2) the detailed study of the morphology and physiology of the rat, with comparisons from other groups of vertebrates; and (3) the broader aspects of biology (eugenics, sociology, psychology and agriculture). No doubt this method of teaching will have an appeal to the average student of zoölogy who is chiefly interested in why he operates as he does; but it is open to question whether the invertebrates are not pedagogically important enough to merit at least a few weeks of attention in an elementary college course.

A Preliminary Study of the Nitrogen Needs of Growing Termopsis. *University of California Publications in Zoölogy, Vol. 36, No. 15.*

By Elizabeth S. Roessler. University of California Press, Berkeley. 25 cents. $7\frac{1}{8}$ x $10\frac{3}{4}$; 12; 1932 (paper).

Some investigators have found that termites are able to live on a diet solely of filter paper and water with no other elements present that are generally considered necessary for life; they have even gone so far as to assert that termites can grow just as normally on pure cellulose as on a diet of wood. Miss Roessler, using more care in experimental technique, found that termites fed on a diet of filter paper, although they did grow, did not do so as rapidly nor as well as those fed on wood. Another interesting result to come out of this study is the fact that instars fed on a filter paper diet do not develop normal wing pads. The author makes the suggestion that

the development of first forms, and hence of other castes, is conditioned by the diet; but the development of wing pads is not necessarily caste development, therefore any general conclusions in this regard would be untimely.

THE FOOD OF PROTOZOA. *A Reference Book for Use in Studies of the Physiology, Ecology and Behaviour of the Protozoa. The Egyptian University Publications of the Faculty of Science No. 1.*

By H. Sandon. Misr-Sokkar Press, Cairo. Piastres 20. $6\frac{3}{4}$ x $9\frac{1}{2}$; ii + 187; 1932 (paper).

This book is the outgrowth of a study on the biological relationships of the protozoa of soil and of sewage disposal works which the author made while at the Rothamstead Experimental Station in England. It is a useful review of present day knowledge of what protozoa feed on, involving the consideration of many questions concerning the physiology and behavior of these forms Among these ancillary topics are the digestive mechanism of protozoa, symbiosis, quantities of food consumed by different forms, requirements of the organism for growth and activity, morphology of the feeding mechanism and stimuli to which the organism can react. In presenting the material the author treats each organism systematically according to order and family. A bibliography of 447 titles is given and author and subject indices.

METHODS FOR THE IMPROVEMENT OF MICHIGAN TROUT STREAMS. *Bulletin of the Institute for Fisheries Research No. 1.*

By Carl L. Hubbs, John R. Greeley and Clarence M. Tarzwell. Institute for Fisheries Research, University of Michigan, Ann Arbor. 50 cents. 6 x 9; 54; 1932 (paper).

This bulletin is a comprehensive survey of problems and questions associated with stream improvement. The practicability of such a project is considered. The planning and carrying out of the work, and the most satisfactory techniques available (dams, deflectors, and covers) are described. A list is given of the materials and equipment needed.

ON TOKOPHRYA LEMNARUM STEIN (SUCTORIA) WITH AN ACCOUNT OF ITS BUDDING AND CONJUGATION. *University of California Publications in Zoölogy, Vol. 37, No. 16.*

By Alden E. Noble. University of California Press, Berkeley. 50 cents. 7 x $10\frac{3}{4}$; 44 + 6 plates; 1932 (paper).

This is principally a cytological study of the life history of *Tokophrya lemnarum* with particular reference to its micronucleus. The internal budding of this protozoon is of interest. Although it was found on the roots of other aquatic plants in abundance, curiously enough *T. lemnarum* was never found on *Lemna gibba.*

THE BED-BUG: *Its Habits and Life-History and How to Deal with It. British Museum (Natural History) Economic Series No. 5. Third Edition, Revised, Enlarged, and Partly Rewritten by Major E. E. Austen.*

By Bruce F. Cummings. British Museum, London. 2d. $5\frac{1}{2}$ x $8\frac{1}{2}$; 27; 1932 (paper).

A third revised edition of this useful little pamphlet (originally published fifteen years ago) on these troublesome insects and how to get rid of them.

PUBLICATIONS OF THE UNIVERSITY OF OKLAHOMA BIOLOGICAL SURVEY. *Volume IV, No. 1. Oklahoma Spiders, by Nathan Banks, N. M. Newport and R. D. Bird. No. 2. Dragonflies of Oklahoma, by R. D. Bird.*

University of Oklahoma Press, Norman. 60 cents. 6 x 9; 57; 1932 (paper).

This bulletin contains lists of spiders and dragonflies collected in Oklahoma and notes on common Oklahoma spiders.

AMPHIBIANS AND REPTILES FROM LOWER CALIFORNIA. *University of California Publications in Zoölogy, Vol. 38, No. 6.*

By Jean M. Linsdale. University of California Press, Berkeley. 35 cents. 7 x $10\frac{3}{4}$; 42; 1932 (paper).

DESCRIPTIONS OF NEW BIRDS FROM OREGON, CHIEFLY FROM THE WARNER VALLEY REGION. *Scientific Publications of the Cleveland Museum of Natural History, Vol. IV, No. 1.*

By Harry C. Oberholser. Cleveland Museum of Natural History, Cleveland. $6\frac{1}{4}$ x $9\frac{1}{4}$; 12; 1932 (paper).

New Mammals from St. Lawrence Island, Bering Sea, Alaska. *University of California Publications in Zoölogy, Vol. 38, No. 9.*

By E. Raymond Hall and Raymond M. Gilmore. University of California Press, Berkeley. 25 cents. $7\frac{1}{8}$ x $10\frac{3}{4}$; 12 + 2 plates; 1932 (paper).

A New Lake-Side Pocket Gopher from South-Central California, *by Joseph Grinnell.* A New Pocket Gopher from New Mexico, *by E. Raymond Hall. University of California Publications in Zoölogy, Vol. 38, Nos. 10 and 11.*

University of California Press, Berkeley. 25 cents. $7\frac{1}{8}$ x $10\frac{3}{4}$; 10 + 1 plate; 1932 (paper).

BOTANY

Anthokinetics. *The Physiology and Ecology of Floral Movements. Carnegie Institution of Washington Publication No. 420.*

By G. W. Goldsmith and A. L. Hafenrichter. Carnegie Institution of Washington, D. C. \$3.00 (paper); \$4.00 (cloth). $6\frac{3}{4}$ x 10; iv + 198; 1932.

Beginning their studies in each case with observations on floral movement in the field, Goldsmith and Hafenrichter proceeded to laboratory examination of nearly a hundred species, drawing their material from a mountainous region where a variety of types of floral behavior was to be found.

Under constant conditions such as were employed in the present study, flowers generally show periodic opening and closing movements during the first 24 hours after removal from the field. That is, the general features of the daily behavior of these flowers were predetermined for at least one day after removal from the field and subjection to constant conditions. . . . The strength of periodicity, as measured by the degree of maximum expansion and rate of movement under constant conditions and in response to temperature changes, differs greatly in the different forms. In the flowers of *Taraxacum* and similar forms, periodicity is strong and modifies all floral movements, even after the flowers have been kept under constant conditions for several days. In the flowers of *Tulipa*, periodicity is weak and can easily be overlooked since stimuli of moderate intensity entirely mask it.

The authors made detailed studies of the influence of temperature, light, and humidity on the opening and closing of flowers, but always with reference to their natural periodicity.

There is a rather complete literature review which helps to make this a valuable contribution to an old and honorable botanical problem.

Methods in Plant Histology. *Fifth Revised Edition.*

By Charles J. Chamberlain. University of Chicago Press, Chicago. \$3.25. 6 x $8\frac{3}{4}$; xiv + 416; 1932.

Handbuch der biologischen Arbeitsmethoden. *Lieferung 389. Ernährung und Stoffwechsel der Pflanzen.* Containing following articles: *Methoden zur Untersuchung der Wasserverhältnisse von Torfböden*, by Karl Malmström; *Die botanisch-mikrotechnischen Schneidemethoden*, by Josef Kisser.

Urban und Schwarzenberg, Berlin. 9 marks. 7 x 10; 159; 1932 (paper).

Handbuch der biologischen Arbeitsmethoden. *Lieferung 393. Ernährung und Stoffwechsel der Pflanzen. Die botanisch-mikrotechnischen Schneidemethoden.*

By Josef Kisser. Urban und Schwarzenberg, Berlin. 11 marks. 7 x 10; 206; 1932 (paper).

The fifth edition of Chamberlain's textbook has been thoroughly rewritten and enlarged. Some new techniques for sectioning wood are described and there are new sections on photomicrography, including the use of motion picture equipment.

Kisser has prepared an exceedingly detailed description of the techniques of imbedding and section-cutting of plant material which should be very useful to any plant histologist. Fixation and staining are not discussed.

The methods of investigation which Malmström has developed for the study of peat soils should be useful in work on other soil types.

Plant Sociology. *The Study of Plant Communities. Authorized English Translation of Pflanzensoziologie.*

By J. Braun-Blanquet. Translated, Revised and Edited by George D. Fuller and Henry S. Conard. McGraw-Hill Book Co., New York. $4.50. 5⅞ x 9; xviii + 439. 1932.

Sometime when someone writes the much needed *Dictionary of Ecological Nomenclature*, it will have to be explained that the reason why a term like "sociology" was dragged in was that some ecologists who write textbooks are interested in such things as pollination and seed dispersal and that others aren't; the latter show their interest in plant communities by recourse to picturesque language. What Braun-Blanquet has done is to make a usable and important survey of the recent literature dealing with plant communities and the climatic and edaphic conditions that influence them, writing for advanced students of ecology. Not least of the merits of the book are a bibliography of more than 600 titles and a good index.

CONTRIBUTIONS DU LABORATOIRE DE BOTANIQUE DE L'UNIVERSITÉ DE MONTRÉAL. Nos. 20–21. *No. 20: Quelques Plantes Nouvelles ou Reliquales du Bassin de la Baie des Chaleurs. No. 21: Sur Quelques Ptéridophytes Nord-Américaines.*

By Frère Marie-Victorin. University of Montreal, Montreal, 50 cents. 6 x 9; 29; 1932 (paper).

MORPHOLOGY

CONTRIBUTIONS TO EMBRYOLOGY. *Volume XXIII, Nos. 134 to 138. Carnegie Institution of Washington Publication No. 433.*

Carnegie Institution of Washington. $5.00 (paper); $6.00 (cloth). 9 x 11⅝; iii + 266 + 26 plates; 1932.

This volume contains five papers. The first—Studies in the reproduction of the monkey *Macacus (Pithecus) rhesus*, with special reference to menstruation and pregnancy,—by Carl G. Hartman, is especially important. Over 700 menstrual cycles are recorded. It is found that ovulatory and non-ovulatory cycles are followed by approximately the same amount of bleeding, and that the same individual, with regular menstrual rhythm, may alternate ovulatory with non-ovulatory cycles. Ovulatory cycles are more prevalent in the winter than in the summer months, a fact which seems to demonstrate a breeding and a non-breeding season for the rhesus monkey. The optimum conception day is found to be the end of day 13 or the beginning of day 14. The gestation span was studied and found to vary with the physique of the individual—the more vigorous individuals keeping the fetus longer. The average period of gestation is 164 days.

The second paper, by George B. Wislocki—On the female reproductive tract of the gorilla, with a comparison of that of other primates—is also of great importance. The results of this study support the statement that, from the standpoint of reproduction, man shows the closest anatomical relationship to the anthropoid apes and not to the catarrhine or platyrrhine monkeys. The resemblance is closest in connection with the internal reproductive tract and with placentation.

The third paper—Observations on the bones of the skull in white and negro fetuses and infants—by Marciano Limson, presents the results of a study made of the significant variations and anomalies found in 163 skulls selected as showing no evident symptoms of disease of white and negro fetuses and infants. Anomalies are found to be much more common in fetuses than in adults. All of the variations and anomalies found in the fetuses are known to exist in adults, which suggests the conclusion that such conditions in adults originate during prenatal development.

The other papers in this volume are: The living egg and early stages of its development in the guinea-pig, by Raymond R. Squier; and A presomite human embryo with a definite chorda canal, by Chester H. Heuser.

PHYSIOLOGY AND PATHOLOGY

VITAMINS: A SURVEY OF PRESENT KNOWLEDGE. *Medical Research Council Special Report Series, No. 167.*

Compiled by a Committee appointed jointly by the Lister Institute and Medical Research Council. His Majesty's Stationery Office, London. 6s. 6d. net. 6 x 9½; 332; 1932.

This is the third survey on vitamins which has been issued by a committee appointed by the English Medical Research Council and the Lister Institute. The first is a *Report on the present state of knowledge concerning accessory food factors (vitamins)* and was issued in 1914. The second, a completely new edition, appeared in 1924. In the last survey, commenced in 1930, again a wholly new undertaking was necessary in order to keep pace with the rapid development of the subject. The report will be valuable to instructors, investigators and practicing physicians. The latter will find the sections on "Vitamins and human diets" and "Vitamins in the diet of mother and infant" especially useful. The survey has been made with care and is well documented. The list of references runs to something over 1,500 titles. In Appendix I will be found a table giving the distribution of vitamins in foodstuffs, etc. In Appendix II is given the "Report of the conference on vitamin standards held at London from June 17th to 20th, 1931." In the text are given photographic reproductions of children showing vitamin deficiency, growth curves, charts and tables. There is an index.

A REPORT ON TUBERCULOSIS *Including an Examination of the Results of Sanatorium Treatment. Reports on Public Health and Medical Subjects No. 64.*
By Arthur S. MacNalty. His Majesty's Stationery Office, London. 3 shillings net. 6 x 9⅝; viii + 172; 1932 (paper).

This is a comprehensive study of the present position concerning the prevention and treatment of tuberculosis in England, dealing especially with the sanatorium and the results of such treatment. In 1911 there were 53,120 deaths from tuberculosis. In 1930, there were 35,745. That the problem is one of great complexity and that the goal of complete success is not yet in sight this report deeply testifies. It is shown how contact infection, industrial occupations, urbanisation, overcrowding, poverty, lack of proper nutrition and other diseases favor tuberculosis, and how a return to natural conditions enables the human body to resist tuberculosis. The battle, however, against this devastating disease is not so simple as it was at one time thought to be. It is "only by co-ordinated progress along various paths and by surveying the complex problem as a whole that tuberculosis is likely to be combated successfully."

HANDBUCH DER BLUTGRUPPENKUNDE.
Edited by Paul Steffan. J. F. Lehmanns Verlag, München. 48 marks (paper); 50 marks (cloth). 6⅝ x 10; xi + 669; 1932.

A comprehensive review of the research on blood-groups which has been done since the discoveries of Landsteiner in 1901. The book is divided into nine parts. Dr. Michael Hesch contributes Part 1, on the development of research on blood-groups, and Part 9, a bibliography of about 3,000 titles. Part 2, on the serology of blood-groups of man and animals, is contributed by Oluf Thomsen; 3, on the inheritance of group determined properties of the blood, by Siegmund Wellisch; 4, the relations between blood groups and other hereditary characters, especially abnormal conditions, by Oluf Thomsen; 5, the practical significance of blood-group research in medical treatment, by Heinrich Bürkle-de la Camp; 6, the science of blood-groups in forensic medicine, by Gottfried Raestrup; 7, blood-groups and races of man, by Paul Steffan; and 8, the technic of blood-group determination, by E. D. Schött. In addition to the general bibliography there is, appended to Part 5, a list of over 200 titles dealing with blood transfusion. The book is well indexed.

EPIDEMIOLOGY, *Historical and Experimental. The Herter Lectures for 1931.*
By Major Greenwood. The Johns Hopkins Press, Baltimore. $1.50. 5¾ x 8¾; x + 80; 1932.

In the first of these lectures the history of epidemiology from Hippocrates to Ross and Brownlee is outlined. The second and third lectures are devoted to the author's pioneer work in experimental epidemiology, from which he concludes that "if

healthy immigrants are admitted to an infected herd, even if infected immigrants are rigorously excluded, the herd sickness will recur although intervals of apparent freedom may be so long that the disease will seem to have died out" and that "pre-immunised animals suffer a lower mortality than non-immunes, but that in a herd recruited wholly from pre-immunised animals the disease does not die out." Thus, while pre-immunisation is an invaluable means of reducing the mortality of persons exposed for a short time to great risks, it cannot take the place of environmental betterment. On the other hand, in virus as distinct from bacterial diseases there are reasons for thinking that active immunisation may be an effective prophylaxis.

The material is presented with great charm. It exhibits throughout the wide and profound range of learning, the sound critical judgment, and the polite but sometimes biting irony and wit, for which the author is famed. Altogether this little book is one to be read and pondered over by every public health official for its direct bearings upon his daily business; and by the investigator in any field of biology for its philosophical insight into the difficulties and limitations of scientific methodology.

HANDBUCH DER BIOLOGISCHEN ARBEITSMETHODEN. *Lieferung 387. Allgemeine und vergleichende Physiologie.* Containing following articles: *Die Vitalfärbung des Blutes*, by R. Wolfer; *Die Schaukelextraktionsmethoden*, by Erik M. P. Widmark; *Methoden der Bauchfensterbildung*, by Josef Deutsch; *Mikrogeometrische Messung*, by Keijo Okajima.

Urban und Schwarzenberg, Berlin. 10 marks. 7 x 10; 150 + xx; 1932 (paper).

The articles in this number of the Abderhalden *Handbuch* series deal with the following subjects: the vital staining of blood; shaking methods of extraction (we found pictured one ingenious apparatus constructed from a boy's "Meccano" set); the construction of abdominal windows; and microgeometric measurements of organs and tissues.

BIOCHEMISTRY

THE DONNAN EQUILIBRIA *and their Application to Chemical, Physiological and Technical Processes.*

By T. R. Bolam. G. Bell and Sons, London. 9 shillings net. $5\frac{3}{8} \times 8\frac{3}{8}$; vii + 154; 1932.

The intimate connection of the Donnan equilibria with biological processes may be indicated by a quotation:

> The theoretical considerations detailed in the following lead to the general conclusion that the presence in any system of electrolytes of a species of ion, which is restrained in *any* way from diffusing to all parts of the system, will give rise to unequal distribution of every species of diffusible ion present. This particular state of *unequal ionic distribution* is the characteristic feature of "Donnan equilibria."

Approximately a third of the book is devoted to biological applications of the equilibria. There is an adequate index and a bibliography of 143 titles.

THE BIOCHEMISTRY OF MUSCLE.

By Dorothy M. Needham. E. P. Dutton and Co., New York. $1.25. $4\frac{1}{8} \times 6\frac{3}{8}$; viii + 166; 1932.

A summary of recent discoveries about the process of conversion of chemical energy into the energy of muscle contraction. The author discusses the revolution in the old physiological views of muscle contraction, and the reinterpretation of facts, long known, into a new picture. Most of the chemical work described has been done on frog and rabbit muscle. The assumption is made that these observations can be generally applied to voluntary muscle. There is an extensive bibliography, a good glossary and an index.

ELECTROMETRIC pH DETERMINATIONS OF THE WALLS AND CONTENTS OF THE GASTRO-INTESTINAL TRACTS OF NORMAL ALBINO RATS. *University of California Publications in Zoology, Volume 36, No. 14.*

By Charles A. Kofoid, Ethel McNeil and Relda Cailleau. University of California Press, Berkeley. 25 cents. 7 x $10\frac{3}{4}$; 9; 1932 (paper).

Rats on a relatively low fat diet showed a

practically neutral reaction for the wall of the duodenum and ileum and a slightly alkaline reaction for the caecal wall. The rats tested were not examined for intestinal amoebae, but as other rats living in the same cages showed many amoebae and flagellates in the caecum the authors conclude that a neutral or alkaline range, approximately the pH of the blood, is optimal for the growth of these protozoa of the rat.

WÖRTERBUCH DER KOLLOIDCHEMIE.
By Alfred Kuhn. Theodor Steinkopff, Dresden and Leipzig. 8 marks. $4\frac{3}{4} \times 7\frac{5}{8}$; 179; 1932.

This is something more than a dictionary; it is a sort of small textbook on colloid chemistry alphabetically arranged with graphs, tables, illustrations, and literature references, and it should make life considerably easier for any biologist reading up on colloid chemistry.

SEX

MY FUTURE CHILD AND YOURS. *An Intelligent Program of Improving Life at its Source, Before Conception and in the Womb, Written in a Simple Manner to be Understood by all.*
By Roscoe C. Evans. Roscoe C. Evans, Oklahoma City. $5\frac{1}{4} \times 7$; 238; 1931.

"Intelligent procreation" is the theme of this book. "Intelligent procreation consists" in recognizing, besides heredity and environment, prenatal influence as a third great factor influencing the development of individuals. Prenatal influence, claims the author, occurs whether we are conscious of it or not. The program of intelligent procreation is to influence the unborn child consciously, in the right direction, impressing on it good habits, trends and attitudes. This influence is to be accomplished through the agency of the mother's endocrine glands, but only as a result of both Papa and Mama taking thought and following the author's program of righteous, not to say pious living.

No book has depressed us so much as this in a long time. It has spoiled our day because it is so perfect an exemplification of two great and immutable truths: One, that honesty, sincerity and nobility of purpose are hopeless as substitutes for knowledge, insight and understanding, quite regardless of their value otherwise; the other, that a little knowledge is worse than a dangerous thing, it is devastating.

THE CRITICAL AGE OF WOMAN.
By Walter M. Gallichan. Williams and Norgate, London. 4s. 6d. net. $4\frac{7}{8} \times 7\frac{1}{8}$; 160; 1932.

The author discusses in non-technical language the physical and psychological problems which arise as woman approaches the so-called critical age and shows how neuresthenia and various forms of emotionalism seem to be directly traceable to the improper instruction of young girls in matters pertaining to sex physiology, to unhappy marriages, or unfulfilled desires.

BIOMETRY

FERTILITY AND REPRODUCTION. *Methods of Measuring the Balance of Births and Deaths.*
By Robert R. Kuczynski. Falcon Press, New York. \$1.85. $5\frac{7}{8} \times 9$; 94; 1932.

The experienced and well trained worker in population statistics can read this book without very much harm (except waste of time), for he can correct most of the author's numerous errors as he goes along. But when, on the first page of the text, the author states his purpose: "This book is intended to serve as an introduction into the methods of measuring fertility and reproduction," the unsuspecting beginner deserves a warning against the pitfalls prepared for him. Some of these are mere inaccuracies of algebra, as when, on pages 28, 29, 30, 57, 85, 86, 87, 90, and 91, for example, the wrong sign is attached to certain quantities; or when a formula is plainly garbled, as in the last formula on page 86.

More serious than these formal errors is the muddled thinking which has inspired such passages as the following: On page 28 the net reproduction rate (denoted by R_0) is defined as "female births per female

in stationary population." This statement taken literally has no definite meaning at all, because it does not state the length of time referred to. The reader will naturally suppose, in the absence of any other indication, that the annual births are meant. On this understanding the statement is plainly wrong, for actually the annual number of births per female in a stationary population is the reciprocal of the mean length of life, a figure of the order of .02, whereas R_0 is the ratio of births in two successive generations, a figure which, as a rule, will not depart materially from unity, and which has intrinsically nothing to do with the stationary population. What the author *meant* to say is "female births issuing from a life table cohort of females *in the course of its entire career*, per female entering the cohort at birth." Again on page 34 it is stated that the rate of increase of a stationary population dropped from 10.6 to 6.2 per 1,000. This is plainly nonsense. Another bad blunder is on page 58, last paragraph. The quantities R_1 and R_0 are completely determined by the life table and the age schedule of fertility, and since these are assumed given and constant in the discussion, the ratio $\frac{R_1}{R_0}$ cannot assume two different values, as it is here stated to do.

On page 26 the section "Yearly Rate of Increase Versus Yearly Increase" begins with a muddled title, continues with unnecessary complications, and ends without mentioning the one really significant fact, namely, that a rate of increase computed simply on the basis of the arithmetic mean of the population at the beginning and the end of the year comes within one in 30,000 of the answer found by Kuczynski's complicated formula.

But the prize for confusion of thought belongs, perhaps, to a passage on page 23, where the author remarks: "It is evident, therefore, that if a population is constantly subject to a certain mortality (in each year of age), and if the number of births constantly equals the number of deaths, this population, whatever may be its present age composition, will sooner or later have an age composition corresponding to that of the life table, and from then on will forever preserve this age composition." The fact, of course, is that under the conditions stated the population actually *is* stationary and it is only by the most extraordinary and improbable compensatory fluctuations in the age-specific fecundity that any other than the stable age composition could exist from the very start.

On pages 63 to 64 the author spends nearly a whole page expatiating on an alleged error of Dublin and Lotka, who, in their original paper on the *True Rate of Natural Increase* did not correct their population to the midyear number in computing their fecundity rates. Kuczynski speaks of this as a "serious mistake." The neglect, of course, is not a mistake at all, but the disregard of a minor factor in a computation which, in the nature of things, cannot be very accurate. But the singular thing about this incident is that Kuczynski himself, in another place, omits the corresponding correction in computing fecundity rates for Italy.

The account of Bortkiewicz's 1911 publication (*Die Sterbefrequenz etc. in der stationären und in der progressiven Bevölkerung*) and Lotka's 1907 papers (*Science*, Vol. 26, page 21; *American Journal of Science*, Vol. 24, page 199) and their relative contributions to the subject is wholly misleading. Bortkiewicz did *not* show, (as Kuczynski says he did), how to compute a stable age distribution. To do this requires the determination of the rate of natural increase corresponding to a given mortality and fecundity, and this is found for the first time in the literature in Sharpe and Lotka's paper in the *Philosophical Magazine* of April, 1911. Bortkiewicz did not "start from a stationary population and show what will be its ultimate composition," as stated by Kuczynski on page 41. What Bortkiewicz did show was how to compute the age distribution in a population that *has for years past been* growing in geometric progression, and in this he is quite clearly anticipated by Lotka, 1907. The formulae which Kuczynski refers to as Bortkiewicz's in contrast with Lotka's are all to be found in Lotka's 1907 paper, if allowance is made for perfectly obvious changes in notation and for the use of equally obvious finite summation in place of integrals, such as

inevitably follows in dealing with arbitrary functions.

Kuczynski's recommendations on page 90 regarding the use of what he distinguishes as Bortkiewicz's and Lotka's formulae are baseless, as he has quite failed to grasp the purpose of certain of these formulae, and has equally failed to recognize the identity of others where the two authors differ only in the notation employed. Lastly, to quote only one more of many misleading statements, Kuczynski, on page 91, remarks "whoever does not want to use Lotka's complicated formula . . . must resort to the formula

$$r = \sqrt[\frac{R_1}{R_0}]{R_0} - 1$$

It is significant that Kuczynski quite forgets to state here that the formula so recommended is also Lotka's.

Körperproportionen und Kopfform bei Neugeborenen.

By Erica Kugler. Art. Institut Orell Füssli, Zürich. $6\frac{3}{4} \times 9\frac{5}{8}$; 149 + folding chart + 3 plates; 1932 (paper).

For this inaugural dissertation measurements were made on 500 new-born infants —250 boys and 250 girls— delivered in the Women's Clinic of the University of Zürich. The descriptions of the methods used in taking the various body and head measurements are augmented by some photographs. Tables give the body measurements and indices, head measurements and indices for each infant in the study. Among the conclusions the author reached are the following:

Body length of new-born boys is greater than that of girls. Number of birth and age of parent influences the body size of the new-born; the first-born is usually smaller at birth than later children. Legitimate children are larger at birth than illegitimate. There is no difference in the absolute leg length of boys and girls, but relative to the trunk length the legs of girls are longer than those of boys. The newborn are mesocephalic. Measurements made on the ninth day showed that the skull configuration had regressed considerably, as in this short space of time all head measurements, with the exception of height of face and breadth of the lower jaw bone angle had increased. There is a bibliography.

Anthropometry of Adult Maya Indians. *A Study of their Physical and Physiological Characteristics. Carnegie Institution of Washington Publication No. 434. Paper No. 38 of Department of Genetics.*

By Morris Steggerda. Carnegie Institution, Washington. \$1.25 (paper); \$1.75 (cloth). 7 x 10; iv + 113; 1932.

This study presents a mass of carefully collected anthropometrical data, which has been subjected to the usual biometric treatment. Seventy-seven males and 56 females were measured by the author, thus bringing the total number of Mayan males from whom physical measurements have been obtained up to 600, and females up to 450. The Mayan Indian is in general very stocky. Relative to Jamaican negroes and the descendants of the Dutch Frisian whites who settled early in that region, the Mayan has the broadest chest, the longest lower arm relative to total arm, the broadest hands, the broadest head and face, and the narrowest ear. His metabolism is highest, his pulse rate lowest, and he has the best teeth. There is a series of good photographs and an index.

PSYCHOLOGY AND BEHAVIOR

Death in the Afternoon.

By Ernest Hemingway. Charles Scribner's Sons, New York. \$3.50. $6\frac{1}{4} \times 9\frac{1}{8}$; 517; 1932.

It has long been plain that there is great need for a thorough and comprehensive treatise on the psychobiology of the bull fight. A first class bull fight, with a good bull and a good matador supported by a competent *cuadrilla*, presents an opportunity not elsewhere paralleled to study some of the most profound problems of behavior, both human and animal. The situation is one of conflict, with death and its avoidance as the supreme motivation. Every form of mental activity—cunning, judgment, strategy, reflection, fear, cour-

age, and all the rest—is brought into play. Their resultants are translated into overt physical behavior in such manner as to be perfectly clear to the understanding observer, and all at such a *tempo* that an afternoon will give the philosophical behaviorist material for a month's reflection.

Unfortunately the complete biological treatise on bull fighting has yet to be written. But Mr. Hemingway's *Death in the Afternoon* comes nearer to supplying the deficiency, so far as concerns the English speaking world, than anything hitherto available. To be sure he is not a trained biologist, and consequently has perhaps not fully grasped the significance of some things and wrongly distributed the emphasis about others, but he is a grand *aficionado*. He knows his bull fights and fighters as probably no other Nordic ever did. Furthermore he has done a thorough and scholarly job in this book. It is logically arranged, well documented, supplements the text with pertinent and well executed illustrations, has a superb explanatory glossary of technical terms, and only fails to reach the highest standards of scientific bookmaking in its lack of an index. Furthermore Mr. Hemingway knows his material and its literature at first hand. He has watched and studied thousands of bull fights, and has not only read the book literature on the subject, but also the Spanish journals edited for fans over a period of many years back. He apologizes to competent *aficionados* for the elementary character of many of his explanations, but surely this is unnecessary. We need an elementary textbook before a pedantic monograph.

Hemingway interprets the bull fight, as a whole, from the artistic viewpoint. He sees in it the classical tragedy, its comedy relief furnished by the horses and the picadors, building up a gradual *crescendo* to the climax in the death of the bull. With great plausibility he fits everything that happens into this scheme. But, speaking as one *aficionado* to another, we feel that he would be the first to admit that other equally logical interpretations of the whole performance are possible. For example, the biologist might consistently and logically interpret the formal bull fight as the foreshortened and partly symbolic picture of the life cycle—the struggle for the continued existence of individual and race, wherein the individual fights to keep alive until he has planted the seed for the next generation, but in the end inevitably dies. On this view the charge of the bull at the horse is symbolically substituted for the sexual act, which even in animals is always slightly ridiculous in seeing, and is in fact at once the most thrilling depiction of that tremendous surging virility of the male which keeps the race going, and also the most stirringly erotic action that respectable ladies are anywhere permitted to witness. Were this not a family magazine detailed evidence could be offered in support of this latter point, derived in part from the reactions of the spectators. It is unnecessary to pursue the point further. We want merely to illustrate the wealth of material for the inquiring mind offered by bull fighting and Hemingway's book about it.

Any book by Hemingway needs no recommendation to the general reader. But we do want to recommend this particular book to biologists. It will give them a lot to think about. Until our own treatise on the *Biology of Bull Fighting* appears—and pressure of other work necessitates the postponement of its writing to our declining years which are already in part mortgaged to the bringing out of a projected *Natural History of Copulation* in elephant folio with numerous plates—we predict that Hemingway's will remain the unchallenged standard work on the subject.

PHANTOM FAME. *The Anatomy of Ballyhoo. By Harry Reichenbach as Told to David Freedman. Noel Douglas, London; Simon and Schuster, New York.* 7s. 6d. net (England); $2.50 (U. S. A.) $5\frac{1}{4} \times 8\frac{1}{4}$; 258; 1932.

This amazing autobiography of the late Harry Reichenbach, "the greatest press agent in America" is not only intensely interesting reading, but also a revealing and almost incredible document on human psychology and behavior. It is the delineation of a career, starting in circuses, street carnivals, and such like shows; and cul-

minating in international recognition in the fields of publicity and organized propaganda. Harry Reichenbach developed his own knowledge of ballyhoo, "the gentle art of fooling the other fellow." He operated on the simple but sound hypothesis that in this day and age the success of any project or person is determined less by inherent capacity or quality than by properly manipulated publicity. On this philosophy he became the most valuable press agent of the infant motion picture industry. His activities in this connection, especially in raising unknown actors and actresses to stardom are particularly illustrative of how potent publicity can really be. He gives an interesting account of the reactions of the stars to their publicity-built reputations—their phantom fame; of the inflated egos which appear, the temperaments which develop and the recourse some take to liquor and drugs. In Chapter XII a keen analysis of the power of publicity is given, showing how, by means of press, radio, and film it is possible for 50 people in a metropolis like New York City to dictate the customs, trends, fads and opinions of an entire nation of 120,000,000 people.

The final chapters describe the activities of Reichenbach, and the part of publicity and propaganda in the World War. In the conclusion, David Freedman, his collaborator, writes of him:

> He always kept in the background and was scarcely known by the public at large, but in the arts and industries where he operated, his name was a magic key to all the mysteries of building fame and fortune from the printed word. The motion picture industry is inconceivable without him..... He transformed the rudimentary principles of ballyhoo enunciated by Barnum and other circus pioneers into a philosophy of propaganda.

A grand picture of a great man, the perfect exemplar and fine flower of the civilization that nurtured him!

KONNERSREUTH. *A Medical and Psychological Study of the Case of Teresa Neumann.* *By R. W. Hynek. Translated and adapted by Lancelot C. Sheppard. Burns Oates and Washbourne, London; Macmillan, New York.* 4 shillings net (England); $1.50 (U. S. A.) $4\frac{5}{8} \times 7\frac{1}{4}$; v + 150; 1932.

Remarkable things have been happening to Teresa Neumann, a Bavarian peasant woman and a devout Catholic, ever since she injured her spine in 1918 at the age of twenty. They include a fast of five years duration; the periodic occurrence of raw, bleeding wounds on hands, feet, side, and face every Friday; visions; trances in which she speaks grammatically (more than can be said for Teresa's use of her native language), in a dead language, Aramaic, and a dozen more ordinary calamities.

Her original injury was aggravated by neglect and intensified by a series of severe accidents which finally left her paralysed and blind. Her recovery from this unhappy state is no more remarkable than some of the cures attributed to her. The wounds which appear at the time when she sees visions of the crucifixion of Jesus, bad as they are, are really among the least of her infirmities. The visions are described so vividly and with such a wealth of gruesome detail that at times we were not sure who saw the visions, Teresa or Dr. Hynek.

Since 1927 Teresa has taken no food or drink, except the daily communion. Dr. Hynek stresses the point. On one occasion for two weeks she was kept under continuous observation by four nuns who swore that during that time she received only 39 grams of bread and 45 cc. of water and at the end she weighed exactly as much as she did at the beginning of the two weeks.

If this doesn't interest you in Teresa it surely ought to interest you in Dr. Hynek; he believes all this, and more.

THE PSYCHOLOGICAL EFFECTS OF MENSTRUATION. *By Mary Chadwick. Nervous and Mental Disease Publishing Co., Washington and New York.* $2.00. $5\frac{7}{8} \times 9$; 70; 1932.

We deplore such an extreme Freudian approach to a subject which has not been adequately studied, and about which there exists such a vast amount of pseudoscientific talk. Such quotations as the following make us view the work with scepticism:

> The onset of puberty and the appearance of the menstrual flow awaken former guilt and phantasies

of castration and death to the child, with feelings of hostility to the mother and love to the father, normally, but occasionally this will be reversed. What influence may this have for the subsequent nervous development of the adult woman?

Further the author says:

By way of illustration of some of the points mentioned in this paper, we may include two case histories, which show in their prevailing symptoms, phantasies, dreams and transference manifestations, many of the same phenomena that were considered typical of those women, who were accused of witchcraft, as well as those characteristic of the related overwhelming mother-fixation.

It would be nice to have a sample somewhat larger than two.

PRINCIPLES OF MENTAL DEVELOPMENT. *A Textbook in Educational Psychology.*
By Raymond H. Wheeler and F. Theodore Perkins. Thomas Y. Crowell, New York. \$3.75. $5\frac{1}{2} \times 8\frac{1}{2}$; xxvi + 529; 1932.

This textbook aims "to present a Psychology for Education which relates the facts of experiment to the demand of the growing mind to live not only efficiently but with artistic and moral expression." The authors emphasize the fact that

"Psychology has yet to realize that it is the Science of Human Nature, not the science of sensations, reflexes, mechanical conditioning processes and bundles of urges" . . . . "that man is NOT a machine,"

and

"that the laws of his behavior are the laws of intelligence, will and personality, not the laws of association."

This will be found to be an exceedingly interesting and well balanced book, one in which the authors have not complicated but clarified the situation. Much previous experimental work is evaluated in the light of recent trends of psychological interpretations. Many will disagree with some of the main tenets which the authors hold and future studies will undoubtedly demand a new outlook on this exceedingly complicated subject, but the book trends in the right direction. Each section is well documented, the illustrations are adequate, and there are author and subject indices.

FLUCTUATIONS IN HUMAN OUTPUT. *The British Journal of Psychology Monograph Supplements XVII.*
By S. J. F. Philpott. Cambridge University Press, London. 12 s. 6 d. net. 7 x 10; viii + 125; 1932 (paper).

The problems discussed here are of fluctuations or oscillations in uninterrupted mental work. With the best of intentions, output fluctuates, and these fluctuations can be measured experimentally. The general hypothesis of the study is that output curves are essentially periodic, the waves being geometric in nature, i.e., of constant periods when plotted against the logarithm of time. Evidence in support of this periodicity is presented, and interrelationships between the various wave measures noted. The results seem to substantiate the hypothesis, and the further more fundamental conclusion is drawn that

there are many elementary waves present, their logarithmic periods being whole-number multiples of a given (but as yet unmeasured) unit of logarithmic time, that the said unit is universally true for all our subjects, under all conditions of experiment met with, and that finally, true phase differences from curve to curve seem to be negligible.

There is a bibliography of 37 references.

THOSE SUPERSTITIONS.
By Sir Charles Igglesden. Jarrolds, London. 6 shillings net. $4\frac{3}{4} \times 7\frac{1}{4}$; 240; no date.

This is an amusing catalogue of superstitions common in English-speaking countries. Sir Charles is content to take his tales as he finds them, without criticism or comparison with the superstitions of other races. He is inclined to think many superstitions were originated for personal profit by the witches who were hunted so relentlessly in former times. The foreword contains the warning:

When the legend of hell fire, eternal and actual, fell to pieces, many an honest man's trust in Heaven went with it. We must be careful how we destroy superstitions lest we undermine the very supports which hold above the earth all those who do "not live by bread alone."

An Elementary Psychology of the Abnormal.

By W. B. Pillsbury. McGraw-Hill Book Co., New York. \$3.00. $5\frac{1}{2} \times 8$; x + 375; 1932.

The aim of this book is to give the college student and the general reader an account of those aspects of abnormal psychology that are likely to affect or interest them. The facts and theories of hypnotism, the neuroses, insanity, and feeble-mindedness are presented. There is a concluding chapter on mental hygiene. Like many other academic psychologists the author is critical of Freud and his work.

Gorillas in a Native Habitat. *Report of the Joint Expedition of 1929–30 of Yale University and Carnegie Institution of Washington for Psychobiological Study of Mountain Gorillas (Gorilla beringei) in Parc National Albert, Belgian Congo, Africa. Carnegie Institution of Washington Publication No. 426.*

By Harold C. Bingham. Carnegie Institution of Washington, D. C. \$2.00 (paper); \$3.00 (cloth). $6\frac{3}{4} \times 10$; ii + 66; 1932.

DE OMNIBUS REBUS ET QUIBUSDEM ALIIS

A History of Fire and Flame.

By Oliver C. de C. Ellis. Simpkin Marshall, London. 15 shillings net. $4\frac{5}{8} \times 7\frac{1}{2}$; xxiv + 440; 1932.

Intelligent men in other times than our own have felt more or less clearly the need for fundamental concepts akin to our ideas of solid, liquid, gas, and energy, and to fill this need they have evolved a bewildering variety of concepts, related, so Dr. Ellis implies, by a common necessity for clarity in thinking about nature. These concepts did not remain the property of wise men and natural philosophers; they were taken over by the common people, distorted and given new values, and the properties, real and imaginary, of earth, water, air, and fire (the fore-runners of our physical concepts), became matters of ritual and belief and so shaped human conduct mightily. Ellis has undertaken to show, by collecting and collating bits from the literature of antiquity, fragments of folk-lore, and materials with which the scientific community is more familiar, how these fundamental concepts developed. No other kind of book, except a dictionary, could refer learnedly to as many kinds of knowledge in one volume as this one. Suppose, for instance, we list the items that fall under Q in his index: Quakers, qualities, Quanta, Quantitative treatment, Quenching, Quern, Quetzalcoatl, Quicksilver, Quiller-Couch, Quills, and Quintessence; there are about 5000 other items in the index as diverse as these. His concluding chapters deal with modern views on the nature of flame and explosions and are illustrated by photographs of exploding gas mixtures taken at 20 millisecond intervals.

We have tried to outline the central thesis of the book, but it would be misleading to say it is the most important feature, either to Dr. Ellis or to the reader. It so happens that the pleasantest feature of the book is the same one that makes it hard to follow; an uncontrollable tendency to wander away from the argument into a maze of anecdotes, extended quotations from mediaeval treatises, and little oddities of all descriptions. It wouldn't be the entertaining book it is without this glaring weakness.

Pistol v. Poleaxe. *A Handbook on Humane Slaughter.*

By Lettice Macnaghten. Chapman and Hall, London. 21 shillings net. $5\frac{1}{2} \times 8\frac{1}{4}$; xxv + 577; 1932.

A comprehensive and well-illustrated book in which the author has summarized almost all of the literature which has appeared in the last twenty years on the subject of humane slaughter of food animals, and puts in her plea for the compulsory use of humane killing instruments in Great Britain. Although many towns in Great Britain have passed laws on slaughter-house reform and the pistol is in pretty general use where cattle are killed, there are still a large number of towns which refuse to do so. This is especially true in districts where large numbers of sheep and pigs are killed as it has been found to be

almost impossible to adopt mechanical stunning before cutting the throat of the animal on account of the "splashing" which occurs in a high proportion of cases, and because of the difficulties which are met with in the curing and preservation of the flesh. These difficulties have been overcome in Continental Europe where an electric device is being used with some success. This device has the added advantage of doing its work silently—even on pigs. However, Miss Macnaghten concludes her views, given in the introduction, as follows:

Attempts are made from time to time to put on the market mechanical killers which are attractive to the trade because they require no cartridge, or for some other reasons. If these killers are passed by the Societies for the Prevention of Cruelty to Animals, we may well rest content. If not, we should demand an investigation, and in the event of the killer not being considered satisfactory, we must press for the old and reliable types to be substituted.

Stunning by electricity is hardly mentioned in this book. My own view is that we already have safe, simple, economical and perfectly humane killers for all requirements. Why trouble about another method, the action of which has the reputation of being most uncertain?

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